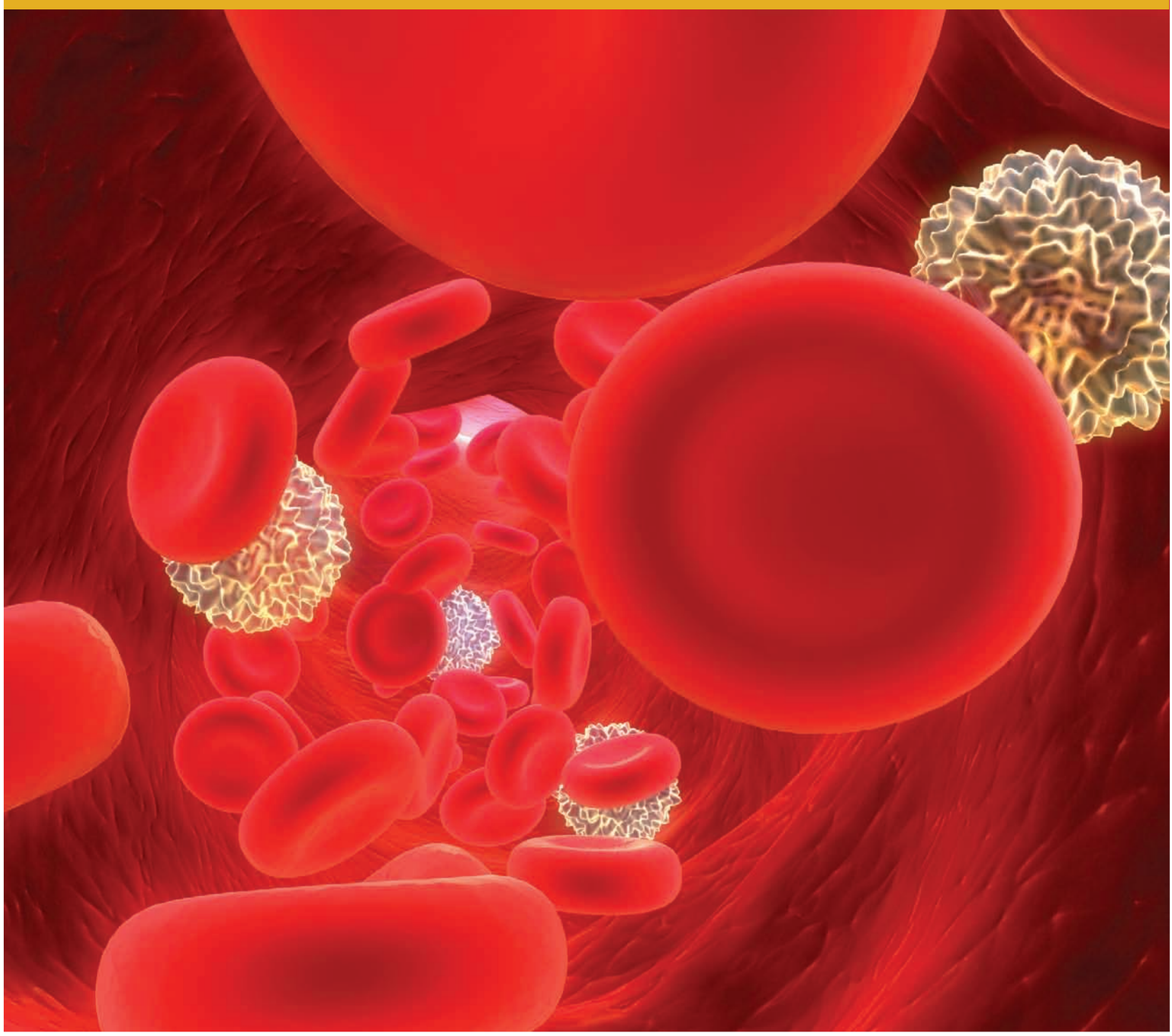
123 Doc EDUCATION

FOUNDATION YEARS JOURNAL

EDITOR IN CHIEF, MICHAEL VASSALLO

Volume 3, Issue 1: Infectious Diseases, Immunology



INFECTIOUS DISEASES, IMMUNOLOGY

Volume 3, Issue 1

Introduction

To celebrate the second anniversary of our **Foundation Years Journal,** we have redesigned and improved the content of our publication based upon feedback from our valued hospital and individual subscribers.

Helping Your Progress Through Your FY Training

To make our journal more relevant and practical for your Foundation Years training, we, in cooperation with leading Foundation Year Directors, have identified seven crucial areas of the MMC curriculum that will help you progress through your training. These new sections, addressed in each issue, are highlighted in blue to the right of this page.

More Succinct & Complex Clinical Articles

Each section will contain condensed, yet more succinct and complex clinical-based articles. We want to ensure you develop a higher level of knowledge as well as intellectual and practical thinking for now and your future specialty training years. The number of "review articles" will be reduced to their minimum as theoretical knowledge can easily be found in textbooks.

You Asked, We Listened

Though we have changed our journal so it is adapted to your learning needs, we have significantly improved our current popular areas you asked for. For instance, we added more picture quizzes so you can test yourself among your colleagues. Professionalism in Practice, Practical Procedures and Patient Management will be developed further. Our team of medical experts also reviewed our classroom teaching notes to guarantee the content remains practical, thought provoking and relevant.

Easier For You To Read & Use

To complement these new sections, we have colour coordinated each section and reformatted the layout. This makes our journal easier for you to read, and to navigate and reference articles for your assessments. Finally we have improved the overall design and will include more pictures illustrating the articles to make your reading experience more enjoyable and informative.

Have Your Say

We are always interested in hearing your feedback on how we can improve our journal to better suit your needs. Email your suggestions to **fyj@123doc.com.** I look forward to hearing from you.

I hope you enjoy our new and improved Foundation Years Journal!

Kind regards,

Sabine Guerry
Managing Director

Good Clinical Care

Good Medical Practice

Teaching & Training

Professionalism in Practice

Patient Management

Practical Procedures

Test Yourself

Designed by Tim Lawrenson Creative.
Please visit www.pure-tlc.com.

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Foundation Years Journal

Foundation Years Journal is an international peer-viewed journal which seeks to be the pre-eminent journal in the field of patient safety and clinical practice for Foundation Years' doctors and educators. The journal welcomes papers on any aspect of health care and medical education which will be of benefit to doctors in the foundation training grade in the UK or international equivalents. The predominant emphasis in **Foundation Years Journal** is on work related to patient safety and in health care education.

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Volume 3, Issue 1: Infectious Diseases, Immunology

Foundation Years Journal is the ONLY journal for Foundation Years doctors and educators, specifically written according to the MMC curriculum. It focuses on one or two medical specialties per month, each issue delivers practical and informative articles tailored to the needs of junior doctors. The journal closely follows the Foundation Yearssyllabus to provide the best educational value for junior doctors. In addition to good clinical and acute care articles, assessment questions give junior doctors the chance to gauge their learning.The answers will be published in the next issue, but 123Doc will advance answers to clinical tutor subscribers so they can engage their students in the learning process. Each issue provides comprehensive clinical cases for trainees as well as practical teaching assessments for educators. Readers will benefit from:

- **MMC CURRICULAR-BASED CONTENT** to enhance understanding of the core competencies required from future leading doctors.
- **FOCUS ON SPECIALTY-SPECIFIC CLINICAL CASES** each month to form broad subject coverage.
- **ADDITIONAL IN-DEPTH** good clinical and acute care articles aligned with the case-based discussion assessments.
- **TRAINING GUIDE FOR FOUNDATION YEAR (FY)** educators with proposed clinical cases for teaching sessions.
- **PRACTICAL AND INFORMATIVE** articles written by senior doctors and consultants.
- **EXTRA REVISION** with comprehensive assessment. Questions and Picture Quiz.

Upcoming Issues

Vol 3, Issue 2: General Practice, Cardiology
Vol 3, Issue 3: Gastroenterology
Vol 3, Issue 4: Gynaecology, Obstetrics
Vol 3, Issue 5: Urology
Vol 3, Issue 6: Rheumatology, Orthopaedics

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Notice

FOUNDATION YEARS JOURNAL 2009

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Aim & Scope

The Foundation Years Journal is published by 123doc and is aimed at doctors in Foundation training programmes, their educational and clinical supervisors, as well as medical students and other doctors (particularly international medical graduates) who intend to start foundation training in the United Kingdom.

Journal Sections

The journal has been redesigned and various sections have been introduced to map the journal more closely to the foundation programme curriculum. You can view the curriculum from **http://www.foundationprogramme.nhs.uk/pages/home/training-and-assessment.**

The sections are the following:

1. Good Clinical Care (syllabus section 1).
This section deals with various aspects of patient management including history, examination, diagnosis, record keeping, safe prescribing and reflective practice. Articles could also refer to other aspects of care including time management, decision-making, patient safety, infection control, clinical governance, nutrition, health promotion, patient education, public health and ethical and legal issues.

2. Good Medical Practice (syllabus section 2).
Articles could be on learning, research, evidence based guidelines and audit.

3. Training and Teaching (syllabus section 3).

4. Professionalism in Practice (syllabus sections 4,5 & 6).
This section includes relationship with patients, communication skills, working with colleagues, probity, professional behavior and personal health.

5. Patient Management (syllabus section 7).
Articles should be focused on the recognition and management of the acutely ill patients, core skills in relation to acute illness, resuscitation, management of the 'take', discharge planning, selection and interpretation of investigations.

6. Practical Procedures (syllabus section 8).

7. Test Yourself
The intention is to provide a vehicle whereby trainees and educational supervisors can present original and review articles mapped against the foundation curriculum.

Submission Of Manuscript

All articles submitted to the Journal must comply with these instructions. Failure to do so will result in return of the manuscript and possible delay in publication.

Manuscripts must be submitted exclusively by email (see detailed instructions below). Manuscripts should be written in English of a sufficiently high standard that is intelligible to the professional reader who is not a specialist in the particular field. Where contributions are judged as acceptable for publication, the Editor or the Publisher reserve the right to modify the manuscripts to improve communication between author and reader. Authors whose native language is not English are strongly recommended to have their submissions checked by a person knowledgeable of the language. If extensive alterations are required, the manuscript will be returned to the author for revision.

Covering Letter

The manuscript must be accompanied by a covering letter bearing the corresponding author's signature. Papers are accepted for publication in the Journal on the understanding that the content has not been published or is being considered for publication elsewhere. This must be stated in the covering letter. If authors submit manuscripts relating to original research in the field of education, the corresponding author must state that the protocol for the research project has been approved by a suitably constituted Ethics Committee and that it conforms to the provisions of the Declaration of Helsinki (as revised in Edinburgh 2000), available at **http://www.wma.net/e/policy/b3.htm.** All investigations involving human subjects must include a statement that the subject gave informed consent and patient anonymity should be preserved.

The covering letter must contain an acknowledgement that all authors have contributed significantly and that all authors are in agreement with the content of the manuscript.

Authors should declare any financial support or relationships that may give rise to a conflict of interest.

Submitting A Manuscript

Manuscripts should be submitted by email to **(agnes@123doc.com).** We do not accept manuscripts submitted by post. Corresponding authors must supply an email address as all correspondence will be by email. Authors should use double spacing when submitting their manuscript. Two files or documents should be supplied: the covering letter and manuscript. The covering letter should mention the title, authors, their contribution, provenance, journal section where their work is to be considered (see above) and any conflict of interests. Please supply the files in Word 2003 format.

Figures should be supplied as a separate file, with the figure number incorporated in the file name. High-resolution figures (at least 300 d.p.i.) saved as jpeg files should be submitted.

Manuscript Style

Unless otherwise stated manuscripts should follow the style of the Vancouver agreement detailed in the International Committee of Medical Journal Editors' revised 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication', as presented at **http://www.ICMJE.org/.**

Abbreviations
Abbreviations should be used sparingly to facilitate reading the article by reducing repetition of long, technical terms. Initially you must use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation only.

Units
All measurements must be given in SI or SI-derived units.

Trade Names
Drugs should be referred to by their generic names, rather than brand names.

References

All articles must be referenced appropriately. To reference the journal please use the following abbreviation FYJ-123Doc. (The Vancouver system of referencing should be used and some examples are given below).

References should be cited using superscript Arabic numerals in the order in which they appear. If cited in tables or figure legends, number according to the first identification of the table or figure in the text.

In the reference list, the references should be numbered and listed in order of appearance in the text. Cite the names of all authors when seven or more list the first three followed by et al. Names of journals should be abbreviated in the style used in Index Medicus. Reference to unpublished data and personal communications should appear in the text only.

References should be listed in the following forms:

Journal Article
Vassallo M, Vignaraja R, Sharma JC, et al. The Impact of Changing Practice on fall Prevention in a Rehabilitative Hospital. The Hospital Injury Prevention (HIP) Study. J Am Geriatr Soc 2004; 52:335-9. Book Azeem T, Vassallo M, SamaniNJ. Rapid review of ECG interpretation. London UK: Manson Publishing 2005.

Chapter In A Book
Martin GM. Biological mechanisms of ageing. In: Grimley Evans J, Franklin Williams T eds. Oxford Textbook of Geriatric Medicine, 1st edn. New York: Oxford University Press 1992; 41-48.

Journal Article On The Internet
british Geriatrics Society position paper. Dementia ethical issues **http://www.bgs.org.uk/Publications/Position%20Papers/psn_dementia_ethics.html.**

Tables
Tables should be self-contained and complement, but not duplicate, information contained in the text. Number tables consecutively in the text in Arabic numerals. Table should be double -spaced and vertical lines should not be used to separate columns. Column headings should be brief, with units of measurement in parentheses; all abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, should be used (in that order) and *, **, *** should be reserved for P-values. The table and its legend/footnotes should be understandable without reference to the text.

Line Figures
Line figures should be sharp, black and white graphs or diagrams, drawn professionally or with a computer graphics package. Lettering must be included and should be sized to be no larger than the journal text.

Colour Figures
We encourage authors to submit colour figures and graphics that facilitate the comprehenion of the article.

Figure Legends
Type figure legends on a separate page. Legends should be concise but comprehensive - the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement. The journal accepts the following types of articles (as title please):

Case based Discussion
(CBD - Same Format As Practical Procedure & Audit Please)
These are mainly intended for inclusion in sections 1 and 5 as highlighted above and should be about 1000-1500 words long. The CBD can focus on various aspect of patient care such as presentation, treatment or prescribing. The articles should include areas that are evaluated in the case based discussion assessment tool of the foundation programme .

The manuscript should be set out in the following sections:

- Abstract: this should refer to salient points from the case being presented together with a mention of what aspects are being discussed
- Case History: this relates to theinitial presentation and should include the clinical setting, clinical problem, investigations and treatment. The history section should also include an ongoing update (eg 2 days later, a week later etc) of patient progress and management
- Discussion. This section should include a critical analysis of patient management in relation to clinical assessment, investigations, differential diagnosis, treatment, follow-up, professionalism and clinical judgement. The discussion should also include a discussion about the ongoing management issues and decisions. It is important to note that the case based discussion is not a review of a particular condition.
- Two best of 5 MCQs to be included in the Test yourself section, with answers and detailed teaching notes explaining the answers. The answers only are NOT sufficient and it should be kept in mind when writing the teaching notes that the reader may take the test questions independently from reading the article.

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Authors writing a case based discussion should not write a short history and then write an article about the condition that the patient presented with. Such information can easily be obtained from a text book and is not the scope of journal. Case based discusions written in this style will be returned to the author without being published.

Practical Procedures

Manuscripts on practical procedures should be about 1000 – 1500 words long. They should be set out in the following sections:

- History. This should describe the presentation of the patient and mention why or how the patient ended up needing the procedure.
- The procedure itself. This should include
- indications and contraindications
- explaining the procedure to the patient (including possible complications) and gaining informed consent for procedures
- preparing the required equipment, including a sterile field
- position the patient and give premed/sedation or local anaesthesia as required and involving the anaesthetist where appropriate
- safely disposing of equipment, including sharps
- documenting the procedure, including labelling samples and giving instructions for monitoring and after care
- recording complications and the emergency management of such complications when appropriate.

Adequate pictures and diagrams need to be supplied in order to make the procedure as clear as possible.

Two best of 5 MCQs for inclusion in the test yourself section, including answers and detailed teaching notes. The answers only are NOT sufficient and it should be kept in mind when writing the teaching notes that the reader may take the test questions independently from reading the article.

Audit

Manuscripts, 1500 – 2000 words long, on audit are encouraged. The journal will only publish high quality audit i.e. completed audit cycles or audits that have led to guideline development. Part 1 audits or surveys will not be accepted for publication.

Review Articles

We are interested in review articles on any aspect of the curriculum that is of relevance to our readership. They should be a maximum 3000 words long, 30 references, 250 word structured abstract, 4 tables OR figures.

We would consider reviews on any of the following:

- Good Medical Practice
- Teaching and Training
- Professionalism
- Medical reviews subject to prior discussion with the editorial team as to the appropriateness of the article

Shorter Reflective Practice Articles

We are always pleased to receive short pieces of a thoughtful nature that describes the personal or professional experiences of colleagues working with patients or their relatives. They should have a maximum of 1000 words. As suggested in the Foundation Programme Portfolio (Reflective Practice) these articles should describe:

- What made the experience memorable?
- How did it affect you?
- How did it affect the patient?
- How did it affect the team?
- What did you learn from the experience and what if anything would you do differently next time?

Some aspects to be considered in these articles are:

Communication with the patient, ethical issues, aspect of your works with colleagues, probity and honesty, personal health

Research Papers

The Foundation Years Journal would welcome research articles on Medical Education. Other research papers would be considered if thought to be of interest to the readership of the journal. Articles should be written using the following headings (title page, abstract, introduction, methods, results, discussion acknowledgements, references, tables, illustrations legends.). They should be of a maximum of 2500 words of text, plus abstract, 30 references, 3 tables or figures. Manuscripts should include a structured abstracts should have a maximum of 250 words using the headings introduction, methods, results, conclusion. The title page should contain (i) the title of the paper, (ii) the full names of the authors and (iii) the addresses of the institutions at which the work was carried out together with (iv) the full postal and email address, plus facsimile and telephone numbers, of the author to whom correspondence about the manuscript should be sent.

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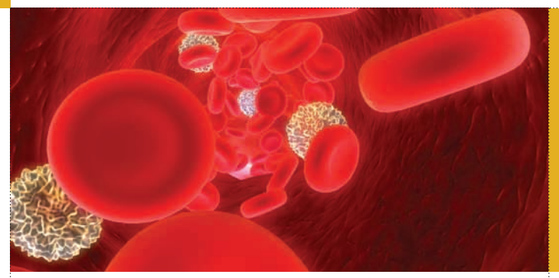
RECENT UK GUIDELINES TO INCREASE HIV TESTING IN HEALTH CARE SETTINGS IMPLICATIONS FOR JUNIOR DOCTORS

Lorraine Peck, Emily Ferenczi and Michael Brown



Approximately 73,000 people in the UK are living with human immunodeficiency virus (HIV) and one-third of these are unaware of their HIV infection[1].
Good Clinical Care.

Introduction

Approximately 73,000 people in the UK are living with human immunodeficiency virus (HIV) and one-third of these are unaware of their HIV infection[1]. As early treatment of HIV can significantly improve morbidity and mortality, and reduce horizontal transmission, it is important to identify this undiagnosed group. This article summarises current policies and research surrounding HIV testing and provides practical advice for Foundation doctors on who, why and how to test for HIV.

The Problem Of Late Diagnosis

In 2006, a British HIV Association audit[1] demonstrated that one-quarter of HIV deaths were in patients who had been diagnosed too late for effective treatment. Certain patient groups are at increased risk of late diagnosis, perhaps as a result of doctors being unwilling to discuss HIV and sexual behaviour. These include heterosexuals, intravenous drug users, migrants from high-prevalence countries and older age groups[2].

Individuals receiving a late diagnosis utilise health care resources more frequently and have an increased number of opportunistic infections than those diagnosed at an earlier stage. Patients with CD4 counts of less than 200 cost the health service twice as much within the first year those diagnosed at an earlier stage[2]. Importantly for the patient, a UK study from 2000 to 2004 demonstrated that earlier diagnosis would have reduced short-term mortality by 56% and all-cause mortality by 32%[3].

It is thought that late diagnosis is also associated with increased transmission rates, due to continued practice of behaviours such as unprotected sexual intercourse, which are usually curbed by an early diagnosis[2].

Routine HIV Testing - The US Approach

In the USA in 2006, universal screening for HIV within all medical settings for patients between 13 to 64 years of age was advocated in regions were seroprevalence was more than 0.1%. Health care professionals were advised to abbreviate the consent process, giving patients succinct information regarding HIV infection and the implication of test results. The "informed consent" for HIV testing was incorporated into obtaining consent for overall medical care. This "opt-out" option increased the number of HIV tests performed in addition to reducing negative connotations associated with HIV testing[4]. Routine testing, using rapid near patient tests, was demonstrated to be feasible in busy emergency departments and acceptable to patients.

Partly inspired by the US experience, in 2007 the UK Chief Medical Officer wrote to all doctors in the UK asking for their help in reducing the public health burden of undiagnosed HIV, with general advice to encourage HIV testing of high-risk patients, and in 2008, national guidelines were introduced[5]. Currently, HIV testing in the UK works on an "opt-in" basis, with the exception of antenatal care and, increasingly, sexual health clinics. A move towards an "opt-out" approach in a wider range of health care settings is now strongly encouraged. One major obstacle to testing is the stigma attached to the HIV test, which could be overcome by making the HIV test more commonplace and thus acceptable among individuals presenting to medical services.

When To Consider An HIV Test?

Junior doctors have an important role in both considering and undertaking an HIV test. They are often the first people to assess acutely unwell medical and surgical patients on presentation to hospital, and attend to these patients regularly during the course of their admission. There are a number of diseases known as "AIDS-defining" where an HIV test is a crucial part of the management of the presenting illness. These include:

- PCP
- Cryptococcal meningitis
- Kaposi's sarcoma
- Cryptosporidiosis
- Presumed cerebral toxoplasmosis
  (i.e. high-risk patients with multiple ring enhancing cerebral lesions)

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Lorraine Peck, Emily Ferenczi and Michael Brown

In addition to these AIDS-defining conditions, the UK guidelines include a list of indicator diseases which may be encountered in routine clinical practice and should raise the suspicion of HIV because they are more common among people living with HIV (see Table 1).

System	Disease
Respiratory	Pneumonia, aspergillosis, tuberculosis
Gastrointestinal	Hep B and C, chronic diarrhoea, oral candidiasis, salmonella, campylobacter, shigella infections
Neurological	Guillian-Barre, peripheral neuropathy, early onset dementia, transverse myelitis, space occupying lesions of unknown origin
Dermatological	Severe/unresponsive psoriasis or seborrhoeic dermatitis
Haematological	Unexplained neutropenia, thrombocytopenia or lymphopenia
Oncological	Head and neck, lung or anal malignancy, lymphoma
Gynaecological	CIN 2 or above
Ear, nose and throat	Chronic parotitis, unexplained lymphadenopathy

Table 1: Indicator diseases.

In addition to patients presenting with indicator diseases, there are lifestyle factors which are associated with HIV and such patients should also be offered a test (see Table 2).

Lifestyle Factors
Intravenous drug use
Males who have sexual contact with other males
Females who have sexual contact with males that have male sexual partners
Anyone diagnosed with a sexually transmitted infection
People who have had sexual contact with individuals from an area where the HIV prevalence is high (e.g. any African country)
Blood or organ recipients

Table 2: High-risk lifestyle factors for which routine testing should be offered.

How Should Consent Be Obtained?

Education on how to obtain consent for HIV testing is not covered particularly well in most Foundation programmes yet it is often the job of the junior doctors to obtain consent and to perform the HIV test. Medical schools emphasise the importance of obtaining consent for HIV testing and in the past it has been taught that lengthy counselling discussions should be undertaken, covering issues such as financial, occupational and future health implications if the test is positive.

The new 2008 guidelines[5] recommend that any trained health professional including doctors and nurses can obtain consent and that a lengthy consent process is not indicated. In particular, health care professionals are encouraged to normalise HIV testing, partly by moving away from obtaining a detailed sexual history unless the consultation requires it. The guidelines emphasise that there are just two essential components which should be addressed:

- The benefits of testing for the individual
- How and where the patient will receive the result

If the patient refuses then reasons for this should be discussed and further risk factors explored as it may be that the patient has misconceived ideas regarding the test or HIV itself. Discussions regarding HIV testing should always be documented in the notes.

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A discussion about HIV testing might go something like this: "You have pneumonia, therefore we need to send off a number of blood tests to look for several things, including your kidney function and some markers of infection. We also routinely test patients with pneumonia for HIV. Pneumonia is common in patients with HIV, often before there are any other features of HIV infection, and finding HIV infection at an early stage will allow us to treat you before it makes you unwell. Do you know what HIV is? Is this OK with you? We are likely to get the result back by tomorrow afternoon. If you are still here, we can give you the result on the ward, however, if you have gone home by then, would you like us to write or telephone you with the result?"

A recent audit at our hospital demonstrated that 15 per cent of patients with indicator diseases who presented to the acute admissions unit were known to have HIV (unpublished data). However, of the remainder, only 20 per cent were tested for HIV. Introduction of a protocol aimed at improving the testing process had very little impact on testing rates. To improve HIV testing and identification of patients with early stage disease, it is likely that a combination of measures is required, including more intensive education and evaluation of testing performance for medical students and junior doctors, coupled with a move towards routine opt-out testing, as has been adopted in the US.

Universal HIV Testing In UK Settings

As mentioned, some services (mainly outpatient, e.g. antenatal or sexual health clinics) already offer routine opt-out testing, and the UK guidelines make a clear recommendation that "universal testing" be offered in:

- GUM or sexual health clinics
- antenatal services
- termination of pregnancy services
- drug dependency programmes
- health care services for those diagnosed with tuberculosis, hepatitis B, hepatitis C or lymphoma

There is also a recommendation that:

"An HIV test ... be considered in the following settings where diagnosed HIV prevalence in the local population ... exceeds 2 in 1000 population:

- all men and women registering in general practice
- all general medical admissions."

The guidelines recognise that this is a more challenging target, and that there is no UK data available on the acceptability and feasibility of such a strategy. Pilot studies are underway to evaluate this approach, which will require additional dedicated staff and robust pathways into care.

Communicating Results

It is the responsibility of the requesting health care professional to ensure that patients are informed of their test results. Delivering the result in person is recommended particularly where:

- patients are admitted to a ward
- English is not their first language
- particularly anxious/vulnerable individuals
- in patients where the result is highly likely to be positive

What To Do If The Result Is Positive

If a test result is positive then the health care professional communicating the result should be aware of local specialist services to which the patient can be referred. Ideally such patients should be seen by an HIV specialist within 48 hours of receiving the result; a quality indicator used in UK HIV services recommends that all patients should be seen within 2 weeks of diagnosis so that long-term care and management plans can be initiated.

Conclusions

- Substantial progress still needs to be made to encourage doctors to perform HIV tests on patients presenting acutely to hospital with indicator diseases.
- Documentation of consent and plans for communicating HIV tests results is very important to ensure that patients are adequately followed-up with appropriate services.
- Junior doctors, who are often responsible for consenting patients for HIV testing, need to understand the new guidelines for HIV testing and changes to the consent process. Education at medical school and in Foundation programmes should reflect this.
- Interventions, such as routine testing of all patients and near patient testing technologies, may be appropriate to facilitate earlier diagnosis in busy acute hospital settings.
- Non-HIV specialists need to be educated in the importance of early HIV testing and the indicator diseases for which HIV testing is highly recommended.

Further Information

"Medical Foundation for AIDS and Sexual Health" provides a broad range of links and useful information regarding HIV and other sexually transmitted diseases, including leaflets and guidance for non-HIV specialists:
http://www.medfash.org.uk

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[5] UK National Guidelines for HIV testing, September 2008. British HIV Association, British Association of Sexual Health and HIV, British Infection Society (available online at: **http://www.britishinfectionsociety.org/documents/GlinesHIVTest08.pdf**).

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If a test result is positive then the health care professional communicating the result should be aware of local specialist services to which the patient can be referred. Ideally such patients should be seen by an HIV specialist within 48 hours of receiving the result.
Good Clinical Care.

PYREXIA OF UNKNOWN ORIGIN

J Hatcher, M Noursadeghi and J Aberdein

Case Presentation

We present a case of a 30-year-old German student who was admitted with persistent fever, weight loss, joint pains and headache. She was originally referred for an oncology opinion by her GP, who was suspicious of an underlying haematological malignancy. She complained of 3-months intermittent fever, night sweats, fatigue and approximately 4kg weight loss. A rash had developed on her lower limbs and she described poorly localised abdominal pain, together with joint pains in her hands, feet and knees. In addition, she reported episodes of severe headache that resolved spontaneously. She had a past history of vitiligo with no significant family history. She took no regular medications, had no allergies, did not smoke and reported minimal alcohol intake. She was not sexually active and had no other risk factors for HIV infection. She had spent 6-months working as an anthropologist in West Africa in 2006. On examination her temperature was 38.0 and she looked comfortable. She was pale with a diffuse petechial rash affecting both her lower limbs. Her spleen was palpable 2 fingerbreadths below the costal margin. Joint examination was unremarkable. General physical examination was otherwise normal.

Initial blood tests found her to be anaemic (Hb 8.5g/dl and MCV 77.4fL) and thrombocytopenic (platelet count $66x10^9$/L) with normal total and differential white cell counts (WCC $5.7x10^9$/L). C-reactive protein (186mg/L) and ESR (101mm in the first hour) were elevated. Having been admitted to investigate the possibility of haematological malignancy, a bone marrow biopsy was performed, but provided no specific diagnosis on histology or microbiological investigation. Positron emission tomography (PET) scanning with fluorodeoxyglucose (FDG) was then performed and showed avid FDG uptake in mediastinal and retroperitoneal lymph nodes. An attempt at ultrasound guided percutaneous biopsy of target lymph nodes failed to obtain sufficient tissue and mediastinoscopy failed to locate significant mediastinal lymphadenopathy. She was discharged pending out patient follow-up.

She was readmitted within a week with severe headache, photophobia and meningism. A lumbar puncture showed mixed lymphocytic/polymorphonuclear cerebrospinal fluid pleocytosis (100 cells – 50% polymorphs), protein 1.0g/dL, glucose 2.3mmol/L (47% of serum glucose of 4.8mmol/L). Magnetic resonance imaging showed non-specific patchy white matter changes throughout the brain that did not enhance. Empirical antibiotic (ceftriaxone 2g bd) and antiviral therapy (acyclovir 10mg/kg tds) was commenced. Her symptoms improved and she was discharged a few days later. During the next month she attended regular outpatient follow-up. Further imaging with combined computerised tomography (CT)-PET scan showed no change in the splenomegaly that was previously noted but reduced lymphadenopathy. The differential diagnoses of lymphoma, tuberculosis and sarcoidosis were considered. A Mantoux test was negative, serum ACE level was low and repeated bone marrow examination showed no evidence of lymphoma. By this time, multiple conventional blood cultures and mycobacterial cultures of blood, CSF, bone marrow and lymph node samples had all shown no growth. Serological tests for ANA, dsDNA, ANCA, HIV-1 and 2, treponema, brucella, histoplasma and borrelia were all negative, as were blood films for trypanosomiasis and malaria. Thyroid biochemistry was normal, LDH 262IU/L and ferritin 201ug/L.

We present a case of a 30-year-old German student who was admitted with persistent fever, weight loss, joint pains and headache. She was originally referred for an oncology opinion by her GP, who was suspicious of an underlying haematological malignancy.
Patient Management.

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In view of the CSF findings, lymphadenopathy and history of travel to Africa a therapeutic trial of anti-tuberculous therapy was instigated, but 6 weeks hence a clinical syndrome of fever, arthralgia and evolving rash (by now a papular rash on her arms) was still evident. Arthralgia and rash can be invoked by pyrazinamide in the treatment of tuberculosis, but since this triad of features was evident at the outset and no definitive diagnosis of infectious or neoplastic disease had been made, the possibility of an inflammatory/immunological disease was considered. Rheumatological review judged her to fulfil major and minor classification criteria for adult onset Still's disease (Table 1). She was started on corticosteroid therapy and anti-tuberculosis treatment was stopped. Her symptoms and laboratory markers of inflammation resolved, and her anti-inflammatory treatment was sustained with azathioprine as the steroid dose was gradually reduced.

This case took 5 months to reach a resolution. Although, the final diagnosis of possible adult Still's disease is rare, the case exemplifies the need for a multidisciplinary (Haematology, Infectious Diseases, Microbiology, Histopathology, Rheumatology and Dermatology) approach in the management of pyrexia of unknown origin (PUO), and the wide repertoire of investigations that are frequently required.

Discussion

Fever is one of the cardinal signs in medicine. On taking a straw poll of colleagues, 37°C is considered a normal temperature, and above 37.5°C to be abnormal. Few of us know the evidence base from which these numbers have emerged, fewer still can comfortably define an expected diurnal, inter-individual, site and method of measurement of variation. For those so interested we have provided a synopsis of the concepts underpinning fever[1]. We are all sure, however, that the presence of fever is an important sign of disease (Table 2). Most febrile illnesses are of short duration, self-limiting and attributed to acute viral infections. The antibiotic era has largely spared the natural history of severe bacterial infection. Every so often, however, there is a febrile illness that just does not go away, and is the focus of this discussion. These cases present great diagnostic challenges in clinical medicine, providing ample opportunity to exercise well honed "physicianly" skill, including close attention to detail and liberal application of those most useful of assessments: the history and examination.

Definition

The original definition of Fever (Pyrexia) of Unknown Origin is taken from Petersdorf and Beeson, with their seminal case series of 100 patients from 1961[2] (Table 3), but has evolved with changes in modern practice and emerging infectious diseases in the wake of the HIV epidemic and use of immunosuppressive therapeutics[3]. PUO was defined as a febrile illness of more than 3-weeks duration in which temperatures exceed 38.3°C on several determinations and no diagnosis is reached after 1 week of inpatient investigation. Most people who have had a prolonged fever, may have had basic microbiological investigations (blood and urine cultures), full blood count and chest X-ray. Some suggest these should be a requisite component of the definition.

Clinical Assessment

History and physical assessments should be based on the differential diagnosis, therefore a risk assessment for infectious diseases is critically important[4]. Basic demographic information: age, ethnic origin, occupation and lifetime geographic exposures may specifically highlight the risk of tuberculosis, leishmaniasis, malaria, typhoid, brucellosis, trypanosomiasis, Q fever, rickettsia, or spirochaetes (treponema, borrelia, leptospiral). In addition, recreational, sexual activity and animal exposure may inform this risk assessment. Past medical history of rheumatic fever, heart valve surgery or recent dental surgery invoke concern about infective endocarditis. Localising symptoms may provide clues for pneumonias, osteomyelitis, vertebral discitis, hepatic abscesses, sinusitis, mastoiditis or septic arthritis. The presence of joint disease and skin rash, or evidence of small vessel vasculitides (skin or conjunctival petechiae and nail fold infarcts) raises concern about rheumatological causes of PUO, there may also be a family history. A thorough drug history may reveal a perpetrating agent. In immunocompromised patients the differential diagnosis is expanded to include opportunistic diseases.

A thorough physical examination is essential. Pyrexia should be documented and in the outpatient setting a temperature diary can be useful. Skin exam may show peripheral stigmata of bacterial endocarditis, or characteristic rashes, such as lupus or syphilis. Percussion of the sinuses (sinusitis), fundoscopy (retinitis), and a full inspection of the oropharynx (tonsillitis, peritonsillar abscess, stigmata of immunosuppression) that are commonly examined inadequately, can yield surprising results. Lymphadenopathy (cervical, axillary, epitrochlear, inguinal) or hepatosplenomegaly, together with night sweats and weight loss are features of lymphoma, although they are also seen in tuberculosis and fungal infections, such as histoplasmosis. Cardiovascular and respiratory examinations will identify pneumonia, pericarditis, or pleuritis. Central nervous system changes may be subtle or florid, and meningism must be looked for. Musculoskeletal abnormalities to be sought would include arthritis, bursitis, psoas abscess and osteomyelitis. A complete examination would include a rectal (prostatitis), breast and vaginal (pelvic inflammatory disease) examination.

Investigations

The likelihood is that basic investigations would already have been done, and may point the physician towards a diagnosis. A neutrophil leucocytosis in the differential white cell count would point towards an underlying bacterial pathogen, and is frequently accompanied with a raised C-reactive protein. Eosinophilia is often associated with lymphoma, drug fever, parasitic infections and vasculitis. Elevated erythrocyte sedimentation rate is common in rheumatological conditions, and should prompt further blood markers if consistent with the history. Antinuclear antibodies (ANA) in high titres are indicative of an autoimmune disease, such as lupus, Sjogrens syndrome or scleroderma. ANCA (antineutrophil cytoplasmic auto-antibodies) are a group of mainly IgG antibodies particularly associated with systemic vasculitides. Serum lactate dehydrogenase is raised in lymphoma, but may be a very non-specific finding. Renal and liver function (hepatitides) should be measured.

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Highest diagnostic yield is gained from microbiological culture, histopathological specimen or strong serological evidence. Cultures of stool, sputum, urine and blood (three sets) must be sent. Histopathological tissue diagnosis may be gained from lymph node, liver or bone marrow biopsies. Broadly, the larger a lymph node is, then the more diagnostically useful it is likely to be. A 2cm lymph node in a patient with no other localisation could be biopsied and return a tissue diagnosis of lymphoma or tuberculosis. There are a multitude of serological tests (EBV, CMV, HIV 1 and 2, hepatitis, leishmania, spirochaetes, brucella, etc.) that can be requested and must be sent to the appropriate laboratory for interpretation.

Imaging should begin with a plain chest or abdominal X-ray. Chest radiography may show hilar adenopathy, diffuse or localised infiltrates, effusions or upper zone abnormalities that may suggest tuberculosis. A CT scan of the abdomen and chest will reveal any deep adenopathy associated with lymphoproliferative disease. This may well be amenable to appropriate biopsy. In addition, CT scanning of the abdomen will reveal any abscess, and this in turn may be amenable to percutaneous drainage. Magnetic resonance imaging[5], Gallium-67[6] and PET (Positron emission Tomography)[7] scans can also be utilised to identify metabolically overactive sites.

Importantly, the most must be made of all invasive specimens taken. Samples should routinely be sent in formaldehyde to histopathology, but also in saline to microbiology where standard, fungal and mycobacterial culture can be performed. In addition, special molecular techniques such as 16S or 18S ribosomal typing or polymerase chain reaction can then be performed if deemed necessary.

Lumbar puncture is indicated in central nervous system dysfunction and meningism, samples should be taken for biochemistry (glucose, protein), microbiology (cell count, gram stain and culture), virology (polymerase chain reaction for herpes or enteroviruses) and cytology (lymphoma).

Many disease entities are diagnosed on specific investigations, as outlined above, but not all diagnoses have a specific test and many are based on a repertoire of common clinical features. Examples include the Dukes criteria for infective endocarditis[8], Duckett-Jones criteria for Rheumatic fever[9] and the American College of Rheumatology criteria for systemic lupus erythematosus[10].

Empirical Therapy

If a pathogen has been identified then specific treatment can be instigated. Empirical treatment is generally not advocated as it will affect diagnostic investigations, however there will be occasions that empirical treatment should be initiated[11], if there is a likely diagnosis from clinical evaluation or a sick patient (sepsis syndrome or progressive organ damage). Examples include anti-tuberculosis medication for cases suggestive of disseminated tuberculosis, steroids for temporal arteritis that may threaten vision or treatment for culture negative endocarditis. The immunocompromised are a specific subset of individuals that require a different approach, empirical antibiotic therapy is essential in the management of febrile neutropenia and local hospital guidelines must be referred to.

Conclusion

With over 200 causes for Pyrexia of Unknown Origin being identified, the above approach is by no means exhaustive. The diagnosis of Pyrexia of Unknown Origin represents one of the most formidable challenges in clinical medicine, but sufficient application of thoroughness and clinical detective work will often reap rewards. Remember, do not just do something, stand there and think about it.

Major	Minor
Temperature of >39°C for >1 wk	Sore throat
Leukocytosis >10,000/mm³ with >80% PMNs	**Lymph node enlargement**
Typical rash	**Splenomegaly**
Arthralgia's >2weeks	Liver dysfunction (high AST/ALT)
	Negative ANA, RF

Table 1: Yamaguchi criteria for classification of adult Still's disease. Presence of 5 or more criteria, of which at least 2 are major (96% sensitivity; 92% specificity).

Highlighted in bold are the criteria that our patient met in the above case discussion.

Abbreviations: ALT, alanine transaminase; ANA, antinuclear antibody; AST, aspartate transaminase; PMN, polymorphonuclear leukocyte; RF, rheumatoid factor; WBC, white blood cells.

Causes Of Fever
Infectious
Neoplastic – lymphoma, renal cell carcinoma etc
Vasculitis – primary or secondary
Drug associated fever – commonly antibiotics
Miscellaneous rheumatological causes, e.g. Adult Still's, Kikuchi's disease
Factitious

Table 2: Causes of fever.

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Definition Of Fever Of Unknown Origin
Illness of duration > 3 weeks
Temperature of >38.3°C on several occasions
With no diagnosis after 1 week of hospital investigation

Table 3: Petersdorf and Beeson[2] Definition of fever of unknown origin.

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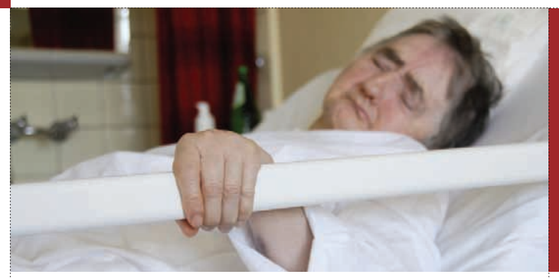
CASE DISCUSSION: A FEBRILE AND CONFUSED PATIENT

Alastair McGregor and Michael Brown



A 66-year-old Caucasian woman, who had worked as a cook before retiring, presented to A&E in a postictal state. She was drowsy and confused and her partner provided the clinical history.
Patient Management.

Introduction

The confused and febrile patient is a staple of acute medical takes. The differential is often wide, ranging from the common but relatively trivial to the rare but life-threatening. Below we present a typical case, discuss the causes not to miss, how to recognise these patients and how to ensure that they are managed optimally.

Case

A 66-year-old Caucasian woman, who had worked as a cook before retiring, was presented to A&E in a postictal state. She was drowsy and confused and her partner provided the clinical history. She had become progressively agitated and confused over the previous 4 days and had complained of a mild headache 48 hours previously that had resolved, although her general neurological state continued to worsen. An hour before her admission to hospital she had a self-terminating generalised tonic-clonic seizure. Her past medical history was unremarkable and her only regular medication was simvastatin. There was no history of travel within the last 6 months but prior to that she had spent 3 weeks in South Africa on safari where she had taken anti-malarial chemoprophylaxis. She was teetotal, a non-smoker, kept no pets and had had no recent illness. There were no identifiable risk factors for HIV.

On examination, her vital signs were unremarkable but she was febrile at 38.4°C. There was no evidence of photophobia or neck stiffness and no rash. She was drowsy and confused, with a Glasgow coma score of 12. There were no localising neurological findings although generalised hyperreflexia and nystagmus were noted.

She did not have papilloedema. Examination of her cardiovascular system, chest and abdomen revealed no pathological findings.

Discussion

The presentation is one of subacute confusion and fever culminating in a seizure. The presence of confusion indicates central nervous system involvement. The nature of this involvement may be primary (i.e. a pathological process involving the brain parenchym) or secondary to a systemic problem). The term encephalitis is used to describe processes that result in primary CNS inflammation whereas encephalopathy generally refers to disturbance of cerebral function that is secondary to other pathologies, which may be infectious, inflammatory, toxic or metabolic in nature

A detailed history and examination, coupled with basic investigations are essential in determining the cause of confusion. Specific causes to consider are listed in Table 1.

Causes Of Fever and Confusion		
Infections	Viral	Herpes simplex type 1 and 2
		Other herpes viruses
		Mumps
		Influenza A
		Enteroviruses (e.g. coxsackie, echovirus)
		Flaviviruses (e.g. Japanese encephalitis, West Nile)
		Togaviruses (e.g. eastern equine encephalitis)
	Bacterial	Tuberculosis
		Brain abscess
		Sepsis
	Protozoal	Malaria
Inflammatory		Behçet's
		Neurosarcoid
		Vasculitis
		Systemic lupus erythematosus
Haematological		Thrombotic thrombocytopenic purpura
Metabolic		Uraemia
		Hepatic encephalopathy
Drugs		Alcohol, recreational drugs

Table 1: Causes of fever and confusion.

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Initial assessment will allow many of these potential causes to be excluded, for instance, the presence of fever makes a toxic or metabolic cause unlikely and many infectious causes would be improbable in the absence of foreign travel. A specific differential that needs consideration is meningitis. This can be distinguished from encephalopathy/encephalitis on clinical grounds. The features of meningitis are photophobia, headache and neck stiffness. Confusion is not generally seen, although elderly patients with any infection may become confused and meningitis may precipitate seizures resulting in postictal confusion.

	Meningitis	Encephalitis
Confusion	not generally	✓
Low GCS	✓ inc. ↑ ICP	✓
Neck stiffness	✓	
Photophobia	✓	
Seizures	✓	✓
Headache	✓	

Table 2: Features of meningitis versus encephalitis.

Case

Blood analysis showed normal liver and renal function. Haemoglobin, white cell and platelet counts were all within the normal range. CRP was 34mg/L and ESR 22mm/hr. Clear lung fields were seen on chest X-ray and urinalysis was negative for nitrites and leucocytes. Unenhanced Computed Tomography (CT) scanning was normal. A lumbar puncture was performed and CSF analysis showed 45 white cells/mm^3 (80% mononuclear cells/lymphocytes), 56 red cells, protein 0.56g/L and glucose of 3.6mmol/L (serum glucose 5.6). A sample of CSF was sent for virology and PCR. A blood film was examined for malarial trophozoites but none were seen.

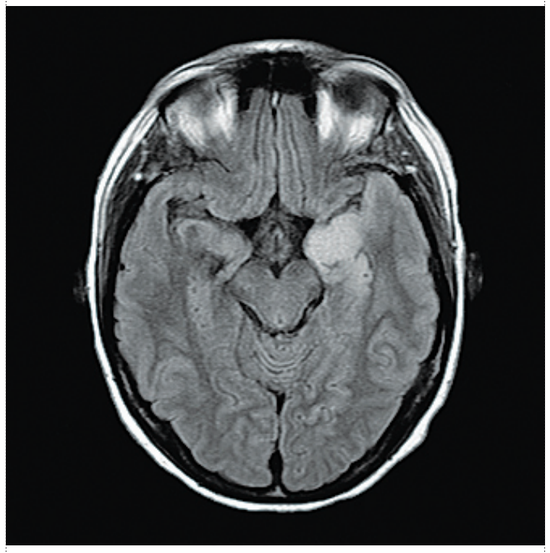
Discussion

Many potential causes of encephalopathy become much less likely in the face of these results. The lack of significant haematological and biochemical abnormalities excludes hepatic and uraemic encephalopathy. The normal peripheral white cell count, together with the X-ray and urine results, makes bacterial infection unlikely. The relatively low ESR goes against vasculitis. Although the CT was normal it was done without contrast and a brain abscess could have been missed. Enhanced CT (or MR) is essential to exclude this important diagnosis. The CSF lymphocytosis would be compatible with viral encephalitis but also with listeriosis, tuberculosis and leptospirosis. However, the relatively normal glucose and protein (and the clinical presentation) would be unusual for these conditions. Cerebral malaria, on the other hand, can certainly behave like this so a travel history, including questions about prophylaxis (and compliance) is vital. Three blood films are usually required to confidently exclude this diagnosis.

The most common viral causes of encephalitis to consider are Herpes viruses (HSV 1 and 2, rarely VZV and CMV) and enteroviruses.

Case

A provisional diagnosis of viral encephalitis was made and the patient was started on aciclovir 10mg/kg TDS. Over the next few days her drowsiness and confusion improved although she remained slightly disoriented and inappropriate. MR scanning of her head revealed temporal lobe signal changes on T2 weighting. (In T2 weighted scans fat, water and fluid give high signal intensity, therefore, T2 weighted imaging is ideal to pick up tissue oedema.)



Discussion

Given the poor prognosis of Herpes Simplex Encephalitis (HSE) and the relative efficacy and safety of aciclovir, commencement of antiviral therapy is recommended as soon as the diagnosis of viral encephalitis is considered[1,2]. The MR abnormalities are highly suggestive, but not diagnostic, of HSE[3]. CT scanning has a sensitivity of only 50% and the presence of CT abnormalities in viral encephalitis suggests severe disease and a poor prognosis[4]. MRI, however, is extremely sensitive in viral encephalitis, particularly in the early stage of disease, with temporal lobe changes indicative of HSE[5].

Case

PCR of the CSF was positive for HSV–1 DNA, confirming the diagnosis of herpes simplex encephalitis. She was treated with 21 days of intravenous aciclovir and made a reasonable clinical recovery, although she still had mild cognitive impairment on discharge.

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Discussion

In most cases of presumed viral encephalitis no pathogen is identified[6] but HSV is the most important cause to exclude as it is usually fatal when untreated. It is also one of the few viral pathogens for which there is a reliable and widely available test. PCR of the CSF is now the gold standard for the diagnosis of HSE and has excellent sensitivity (98%) and specificity (94%) with the sensitivity falling only after 7 days of specific antiviral therapy[7]. Prior to the development of PCR, viral culture of CSF, and culture and immunostaining of brain biopsy material were used to make the diagnosis but, although sensitive, brain biopsy is very invasive and today is only used when the cause of encephalitis is difficult to establish. Measurement of HSV antibodies in the CSF may occasionally be used to make a retrospective diagnosis.

A treatment course of 21 days of aciclovir is currently recommended as shorter courses were found to have a significant relapse rate[8]. It is important to remember that, although relatively safe, aciclovir at high dose can crystallise and precipitate in the kidneys, causing renal failure. In addition, aciclovir can itself cause confusion particularly in the context of renal impairment when toxic concentrations may accumulate. For these reasons, adequate pre-hydration with IV fluids is essential and therapy should be stopped as soon as the diagnosis has been excluded: in patients with normal neuroimaging, CSF cell counts and negative HSV PCR, the probability of actually having HSE is estimated at less than 1% and aciclovir can therefore be safely discontinued.

This case has been used to illustrate the wide differential in a patient presenting with fever and confusion. Common diagnoses include sepsis in the elderly, metabolic and toxic encephalopathy. Rarer causes include brain abscesses, haematological and inflammatory conditions and viral encephalitis. Appropriate use of MR scanning may be helpful in the assessment of patients with viral encephalitis but definitive diagnosis relies on PCR of cerebrospinal fluid.

Herpes simplex encephalitis is a devastating condition when untreated and carries significant long-term sequelae even with optimal management, with one study showing a 1-year mortality of 14% and incidence of chronic neurological deficit of about 20%[10]. A low index of suspicion and prompt empirical therapy remain important in patients with a compatible presentation and appropriate investigation is essential to permit the discontinuation of potentially toxic therapy in those without the disease.

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MANTOUX TESTING

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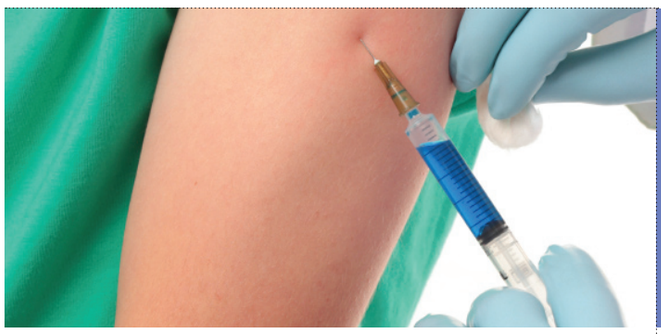

Hold the skin taught. Advance the needle, bevel up, through the skin at an angle of 5–15⁰. The bevel should be covered and just visible through the skin. Relax the pressure on the skin and inject the tuberculin.
Practical Procedures.

Introduction

The Mantoux test (also known as the tuberculin skin test or PPD test) is a diagnostic tool employed in the investigation of tuberculosis infection. It is a skin-based test that produces a measurable reaction. Positive reactions indicate latent tuberculosis infection (LTBI) or previous exposure to mycobacterium tuberculosis. It does not indicate activity of the disease, although this is a common misconception. It is actually negative in approximately 20% of severe disease cases. It has replaced the Heaf test in the United Kingdom as the skin test of choice for tuberculosis infection.

The importance of diagnosing LTBI is derived from the risk that those infected have developing active TB. LTBI in those with a normal immune system brings a 10% lifelong risk of developing an active disease. In the immunocompromised this rises to a 10% annual risk of reactivation[1].

The Mantoux test relies on stimulating an immune response to a non-cell purified protein derivative (hence the term PPD) of cultured inactivated Mycobacterium tuberculosis. Intradermal injection of this tuberculin in the presence of lymphocytes, previously sensitised by exposure to M. tuberculosis, provokes a type 4 delayed hypersensitivity reaction[2]. Clinically this manifests as an area of dermal induration (described below) maximal between 48–72 hours after testing, the size of which is the measured Mantoux reaction.

Indications

The Mantoux test is used in conjunction with history, examination and simple investigations such as chest X-ray in the following broad indications:

Indication	Ref
Contact tracing	2, 3
Entry to country from area of high prevalence	2, 3
Commencing anti-TNF therapy	4
Screening of health care workers	2, 3
Pre-BCG	2, 5

The British HIV Association do not recommend the use of tuberculin skin testing in patients with suspected TB/HIV coinfection or as a screening tool for suspected TB infection in HIV infected patients[6]. It has a poor sensitivity in this patient subset.

Preparation

Discuss the test with the patient covering:

- Safety – it is a very safe procedure
- Test indication – according to case
- Reading – patients will need to return in 48–72 hours for the test to be read
- Side effects – patients may experience some irritation and itching around the site. Very rarely, blistering may necessitate application of topical corticosteroid ointment
- Further management – according to original indication and test result

Procedure

Prepare 2TU of Statens Serum Institute tuberculin in 0.1ml of solution for injection. Use a 26 gauge short bevel needle.

Select a site on the palmar side of the forearm. Pick an area free from scars or markings, as this could impede accurate reading of the test.

Hold the skin taught. Advance the needle, bevel up, through the skin at an angle of 5–15⁰. The bevel should be covered and just visible through the skin. Relax the pressure on the skin and inject the tuberculin. A pale wheal should be formed (expected diameter 6mm–10mm). If the wheal is 5mm or less, the whole procedure should be repeated at a site at least 5cm away.

MANTOUX TESTING

James Richardson, Elspeth Potton and Stephen Morris-Jones

Reading The Test

The measured Mantoux reaction is the radioulnar diameter of tissue induration. (Erythema or soft tissue should be ignored.)

Use a simple ruler to measure the raised tissue. Document the diameter in the notes.

(For a more detailed account visit **http://www.immunisation.nhs.uk/files/mantouxtest.pdf**)[7].

Interpreting The Test

The sensitivity of the test is dependent on an appropriate immune response to the tuberculin, and is unreliable if the patient is immunocompromised for any reason. The specificity is affected by immune exposure to tuberculosis like antigens, the most important of these being previous BCG vaccination.

Mantoux Test	
Sensitivity	77%
False negatives	Immunocompromised: • HIV • Primary immuno-deficiency disorders • Drugs (including steroids, chemotherapy agents and other immunosuppressives) • Elderly • Glandular fever • Active TB disease Others: • Errors in administration • Inter-operator variability • Viral infections including upper respiratory tract • Live viral vaccines (Mantoux test should not be carried out within 4 weeks of a live viral vaccine) • Sarcoidosis
Specificity	59%
False positives	• BCG • Exposure to other mycobacteria

The Green Book[5], the Department of Health's guide to immunisations, divides Mantoux test results into three categories:

<6mm	Negative
6mm – <15mm	Positive
>=15mm	Strongly Positive

A strongly positive test should act as an indication for further investigation for active TB in any patient group. The interpretation of a positive test should take into account the patient's BCG history and their pretest probability of having TB infection.

On initiation of treatment, a Mantoux test that was negative as a result of anergy, when repeated is positive.

Assuming the patient has been adequately investigated to exclude active TB the magnitude of the Mantoux reaction may be useful in deciding to treat for possible latent TB. In adults NICE[2] suggests a two component approach:

A) The patient should be below 36 (because of increasing risk of hepatotoxicity with age)

OR

Be any age with HIV

OR

Be any age and a health care worker

AND

B) Have a positive Mantoux (>6mm) without prior BCG vaccination

OR

Have a strongly positive Mantoux (>15mm) with prior BCG vaccination

AND

a positive interferon gamma test

MANTOUX TESTING

James Richardson, Elspeth Potton and Stephen Morris-Jones

Interferon Gamma Release Assay (IGRA)

The tuberculin test suffers from poor specificity in a population that has been vaccinated with BCG or has a significant exposure to environmental non-tuberculosis mycobacteria. Exploration of the Mycobacterium tuberculosis genome has led to the identification of antigens not found within BCG or most non-tuberculosis mycobacteria. Commercial interferon gamma assays for antigens, such as CFP-10 and ESAT-6, are now available. They have been shown to have good sensitivity and specificity in a BCG vaccinated population[8,9]. The immunological tests detect cell mediated immune responses (T helper type 1) in the host cells to tuberculosis-specific antigens.

Identification of false negatives in the immunocompromised with this form of testing, is achieved by the inclusion of a control that indicates when the test has failed due to poor lymphocyte function.

IGRA-based testing has been assessed in high-risk groups and have been shown to have a higher specificity for exposure in these populations[8,9]. However, longer term longitudinal studies are required to confirm correlation with subsequent disease. Further research remains to be done to validate the tests in other populations[10]. The effect of other factors, including antibiotic therapy, on immunological tests is also not understood.

Tuberculin skin testing is cheap, simple and established. However, studies estimating the cost-effectiveness of the current LTBI assessment tools suggest that IGRAs may be superior to Mantoux testing. IGRAs offer the further logistical advantage over tuberculin skin testing of a single visit assessment. It is quite possible therefore that IFN gamma testing will supersede tuberculin-based skin testing in the future.

Conclusion

For the moment, Mantoux testing continues to be used widely in the assessment of LTBI. Reactivation of latent tuberculosis remains a lifetime risk and appropriate treatment of latent tuberculosis is therefore important for individual and public health reasons. Accurate identification of individuals at risk of LTBI is integral to this decision-making process.

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CAREERS IN INFECTIOUS DISEASES IN THE UK (AND BEYOND)

James Whitehorn and Philip Gothard

In the face of new and emerging infections, such as ESBL-secreting bacteria, XDR-TB and a host of zoonotic viruses, there is an increasing need for pluripotent ID specialists, able to keep up to date with the latest research. Teaching & Training.

Introduction

Infectious diseases (ID) affect all organ systems and all patient groups. Patients can be extremely unwell but with prompt diagnosis and therapy they often get better quickly. For once what we were taught in medical school is true – every patient really is different – and simple skills, such as taking a good history and following-up on clues, is the key to getting their care right. As well as being clinically challenging, ID is traditionally an academic specialty with over half of the 80 or so NHS consultants holding joint contracts with universities.

In the face of new and emerging infections, such as ESBL-secreting bacteria, XDR-TB and a host of zoonotic viruses, there is an increasing need for pluripotent ID specialists, able to keep up to date with the latest research findings while bridging the gap between the lab and the patient's bedside. This overlap between clinical medicine, epidemiology, laboratory science and global health means that a career in ID can take you from high-tech research laboratories to disease control programmes via a PhD and a spell working in settings with poor resources. With such broad opportunities infectious diseases is without doubt the best speciality within medicine (and no, we are not biased).

Training

Infectious disease training is changing. Clinical (ID/internal medicine) and laboratory (medical microbiology and virology) aspects are likely to merge to form one "infection common stem" such as the programmes now available at UCL and Oxford. However, this is by no means certain and there remain strong advocates for the status quo. Whatever the outcome, entry into specialty programmes will continue to be at ST3 level, following core medical training (CMT), with an expectation that successful applicants will have completed MRCP. This year, the London Deanery will become the first to offer posts in "International Health" with 4 months in supervised clinical practice overseas as part of a 2-year CMT programme.

Current training in ID can be combined with either General Internal Medicine (GIM) or microbiology. ID/microbiology combined training takes 6 years whereas ID/GIM is 5 years. In both cases there is an option of counting 1 year of full-time research towards training. The key differences are that ID/microbiology trainees spend around half of their time based in the laboratory with a requirement to pass MRCPath, whereas ID/GIM trainees spend a minimum of 6 months in the laboratory and have to complete 1 year of high- and 2 years of low-intensity GIM alongside clinical ID training (but no requirement to sit MRCPath).

Technically trainees are no longer required to follow a fixed training period but to demonstrate that they have achieved competency in all areas of the curriculum, in part measured by continuous workplace-based assessments similar to those introduced in the Foundation School. It is likely that an infectious diseases exit exam will be introduced in the near future, although the exact timing and purpose of the exam is yet to be agreed. Up to date information may be available from the trainees' representative of the British Infection Society **(trainees@britishinfectionsociety.org.uk).**

In the UK, HIV patients are looked after by a variety of specialists largely depending on the historical evolution of each centre. In London most inpatient HIV units are run by ID physicians and all trainees are expected to spend time caring for these patients. Elsewhere genitourinary medicine specialists often provide care for a few inpatients and larger number of outpatients on increasingly sophisticated regimes of antiretrovirals.

A few trainees every year decide on sub-specialty accreditation in tropical medicine. This involves completing the Diploma in Tropical Medicine and Hygiene (DTM&H), along with 1 year at a UK tropical centre (Hospital for Tropical Diseases at UCLH, Northwick Park and Liverpool) followed by another year in a prospectively-approved clinical post in the tropics.

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Research

There is enormous opportunity for research both during specialty registrar training and as part of a long-term career. For example, the London Deanery advertises several academic clinical fellowships per year specifically designated for ID trainees. These are awarded to clinical research centres with a strong track record of mentorship; they provide 25% of the salary for research and allow trainees time to develop a PhD proposal. Although not essential the majority of ID trainees spend 2 or 3 years in full-time research before completing clinical training. A few institutions have been awarded clinical lectureships to ensure that promising academics have time to develop these skills further.

There is an enormous variety of opportunity for research ranging from epidemiology, observational studies and clinical trials to laboratory-based studies on pathogenesis and the immune response. It usually takes a while to decide what kind of research interests you, followed by another year or two to prepare a successful proposal, so arrange to meet potential mentors early on in training or you may find you have left it too late.

Working Abroad

One of the attractions of ID is the opportunity to work abroad. While it is not true that most of us were dropouts at medical school (honest), it is surprising how many current ID consultants reached their destination via rather circuitous routes. Many ID doctors spend time working abroad, often in settings with poor resources, before obtaining a training number. This can range from attachments in large teaching hospitals with plenty of support, to working in rural health facilities where there is only one doctor (you!). Others choose to work for non-governmental organisations (NGOs), such as MSF or VSO, in refugee camps and conflict zones. Our main advice is to go only once you have some skills to offer; to go for a minimum of 6 months and to remember that local staff will have far more experience than you in managing the conditions encountered in their hospital. Table 1 has a list of organisations that have further information and opportunities for overseas placements.

Career Prospects

The specialties of infectious diseases and microbiology are changing. The NHS workforce plan predicts that by 2022 the UK will need 170 whole-time equivalent (WTE) ID consultants to ensure 0.83 consultants per 250,000 population (NHS Workforce Plan 2008). With around 100 consultants in post today, this represents an expansion of 58%, however, these figures depends upon district general hospital trusts fully committing to consultant-led services in clinical ID. There are very few NHS jobs in ID alone and so trainees should anticipate working either in ID with an Acute Medicine commitment or in a microbiology lab with a strong ID consultancy service. Academic careers will continue to expand for those few trainees who demonstrate research ability at the highest level.

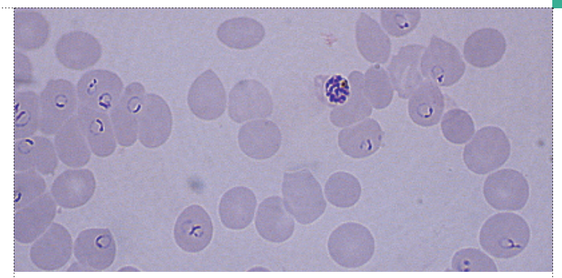

Figure 1: A thin blood film showing trophozoites and a schizont of Plasmodium falciparum. This patient had severe malaria with a parasitaemia of 21.4% and Acute Lung Injury. He made a full recovery with intravenous quinine and ICU support. (Thanks to David Manser, Hospital for Tropical Diseases, UCLH.)

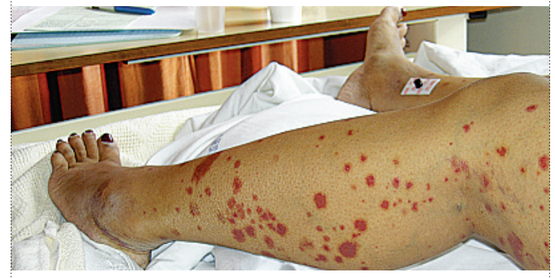

Figure 2: A purpuric rash in a young woman with meningococcal septicaemia. She presented in shock with no signs of meningitis and made a complete recovery with benzyl penicillin and fluid resuscitation. (With permission, Philip Gothard, Hospital for Tropical Diseases, UCLH.)

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Figure 3: A teaching round with one of the authors on ward 4B at Mulago Hospital, Uganda's National Referral Centre. (With permission, Christian Smyth, Kings Fund.)

Society	Website
British Infection Society	www.britishinfectionsociety.org
Royal Society of Tropical Medicine and Hygiene	www.rstmh.org
JRCPTB	www.jrcptb.org.uk
London School of Hygiene and Tropical Medicine	www.lshtm.ac.uk
Liverpool School of Tropical Medicine	www.liv.ac.uk/lstm
Royal College of Physicians	www.rcplondon.ac.uk
Tropical Health and Education Trust	www.thet.org
Medicins Sans Frontieres (MSF)	www.msf.org
Wellcome Trust	www.wellcome.ac.uk
Royal College of Pathologists	www.rcpath.org

Table 1: Links for information and opportunities for overseas placements.

James Whitehorn's Career Path

My interest in infectious diseases and tropical medicine started with an intercalated BSc project looking at malaria and backpacking trips to Asia. I spent my elective working at a hospital in India and saw cases of typhoid, leprosy, malaria and TB. After a medical rotation, which included an HIV job, I worked in rural hospitals in Zambia and Uganda as a volunteer doctor. After returning to the UK, I spent 6 months working as a geriatrics registrar before doing the MSc in tropical medicine and international health at the London School of Hygiene and Tropical Medicine (which included the DTM&H). This was a brilliant year that increased my interest in clinical research. I am now working as an academic clinical fellow in infectious diseases and microbiology at UCLH. I am planning a clinical PhD in the tropics.

Philip Gothard's Career Path

I started life as a career psychiatrist and spent an enjoyable couple of years learning about the doctor–patient relationship and cultural differences in illness behaviour. I was seconded to a Russian research institute for six months and upon returning switched to an SHO medical rotation which happened to include 6 months of infectious diseases. I was inspired by the consultants – they were very cool (unlike the cardiologists) and seemed to have an encyclopaedic knowledge of medicine. After MRCP I spent 3 years as a clinical research fellow working between Oxford and The Gambia, examining the T cell responses to candidate vaccines for malaria.

I moved to London to take up a NTN in infectious diseases and GIM and 5 years later was appointed as an NHS consultant in ID and general medicine at UCLH. The Hospital for Tropical Diseases is a great place to work and with a dozen consultants and six registrars, there is always something interesting happening. My current job consists of 3 months of acute medicine and 3 months on the ward for ID and tropical medicine. I have developed an interest in tuberculosis and run a weekly TB clinic as well as seeing general ID outpatients. I am lucky that my job allows time for international collaboration. I hold an Honorary Senior Lectureship with LSHTM and I am responsible for a capacity-building clinical training link with Mulago Hospital in Uganda.

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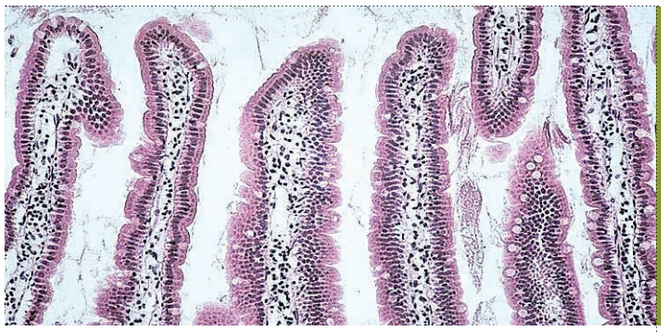
AN AUDIT OF SEROLOGICAL SCREENING FOR COELIAC DISEASE: REAL LIFE MAY NOT QUITE MIRROR RESEARCH?

John Maher, Patrick FK Yong, Edward T Davies and Mohammad AA Ibrahim



A microscopic view of the villi which are severely damaged by gluten in sufferers of the disease.
Good Medical Practice.

Introduction

It has been estimated that up to 1% of the UK population suffer from gluten sensitive enteropathy or coeliac disease (CD)[1]. The condition has a strong genetic basis in that it is associated with the presence of HLA DQ2 in over 90% of cases. Diagnosis requires the demonstration of characteristic histological features in at least one small bowel biopsy, taken from a subject who has been ingesting a gluten containing diet.

It is increasingly appreciated that diagnosis of CD can be fraught with difficulty. The "coeliac iceberg" concept reflects the fact that many CD patients have symptoms not traditionally associated with malabsorption, or indeed may have no symptoms at all[2]. For example, studies of subjects who have asymptomatic anaemia[3] or iron/folate deficiency[4] have revealed that about 1:20 will have undiagnosed CD. Furthermore, the risk of CD is increased in a variety of well-defined situations. These include type 1 diabetes[5], the presence of a first-degree family member with CD[6] and complete IgA deficiency[7]. In light of this complexity, we need robust screening tests to enable physicians to select which patients should undergo small bowel biopsy.

Two serological tests are in common use to screen patients for CD. The first of these detects IgA anti-endomysium antibodies by indirect immunofluorescence microscopy. While this test has served us well, it poses an ethical difficulty (since monkey oesophagus is most commonly used as the antigen source) and requires an experienced observer to recognise the fluorescence pattern. In 1997, the target antigen for anti-endomysium antibodies was identified as tissue transglutaminase (tTG)[8]. Intriguingly, modification of gluten derived peptides by tTG enhances their binding strength to HLA DQ2, thereby linking disease pathogenesis with diagnostic testing. Once tTG had been identified as the key autoantigen in CD, it was natural that ELISA-based tests for antibodies against this target would be developed. Currently, ELISA-based detection of IgA anti-tTG antibodies represents the most commonly performed screening test for CD in diagnostic laboratories.

Quality Standards/Aim Of Audit

Several publications have emphasised the high specificity and sensitivity of IgA anti-tTG antibody positivity for coeliac disease, particularly when human recombinant tTG is used in the diagnostic kit (95–99% in each case)[9, 10]. The British Society of Gastroenterology have commented that "IgG and IgA anti-tTG antibodies can be measured easily and cheaply, using ELISA techniques. They are highly sensitive markers, being present in 90% of patients with untreated disease, and are relatively specific"[11]. Anti-endomysium antibody testing is recognised to be marginally less sensitive, although it may be more specific[9, 10, 12]. In this audit, we have examined the diagnostic performance of the IgA anti-tTG antibody assay for diagnosis of CD in our local patient population.

Methods

A series of 635 requests for serological screening for coeliac disease has been audited (randomly sampled from requests received at the Department of Clinical Immunology and Allergy, King's College Hospital). To screen for possible CD, human IgA anti-tTG antibodies were measured using the Orgentec ELISA kit[13]. Positive results were defined by the cut-off described in the package insert (ten arbitrary units). Total IgA was also measured in order to exclude IgA deficiency as an explanation for a false negative test. This additional test was performed since IgA deficiency occurs in up to 1:80 patients with CD[7]. Results of small bowel biopsies were sought using the King's College Hospital Electronic Patient Record/PathNet systems, at least 10 weeks after the last sample was assayed. Negative predictive value was calculated as the number of true negatives/(number of true negatives + number of false negatives). Positive predictive value was calculated as the number of true positives/(number of true positives + number of false positives). To examine statistical significance, the Mann-Whitney U-test was performed using SPSS software.

Results

Immunoglobulin A anti-tTG antibodies were detected in 20 of 635 screened samples (3.1%). Of the 635 requests, 153 (24.1%) were from the gastroenterology service (4.6% positive); 85 (13.4%) were from the paediatric service (2.4% positive); and 130 (20.5%) were from local general practitioners (1.5% positive).

AN AUDIT OF SEROLOGICAL SCREENING FOR COELIAC DISEASE: REAL LIFE MAY NOT QUITE MIRROR RESEARCH?

John Maher, Patrick FK Yong, Edward T Davies and Mohammad AA Ibrahim

Total IgA measurements were carried out in 624 out of 635 samples (98.3%). Complete IgA deficiency was found in two samples (0.3%). In one further sample, IgA was reported as <0.26g/L. However, a highly sensitive IgA assay was not performed and thus it is uncertain if this patient was truly IgA deficient. Five additional samples had IgA levels below the reference range, but none of these were completely IgA deficient.

Of the 635 patients screened, histological results of a small bowel biopsy (performed at our centre) were found in 55 (8.7%) cases. The IgA anti-tTG assay was negative in 47 of these patients, all of whom had biopsy results that were inconsistent with CD. Thus, the negative predictive value of the IgA anti-tTG test for CD is 100% in this audit.

Only 8 of the 20 patients with IgA anti-tTG antibodies underwent small bowel biopsy in our centre, making meaningful data analysis impossible. To address this, a further retrospective search was performed, in which an additional 50 positive IgA anti-tTG antibody results were identified. Of the resulting 70 patients who were positive for IgA anti-tTG antibodies, records of a locally performed small bowel biopsy were identified in 33 cases. Sixteen of these biopsies revealed a histological profile consistent with CD, whereas the remaining 17 biopsies were inconsistent with this diagnosis. Based upon these data, the positive predictive value of IgA anti-tTG antibodies for CD is 48.5% in this audit. Patients with high levels of IgA anti-tTG antibodies were significantly more likely to have biopsy findings that were consistent with CD (see Figure 1).

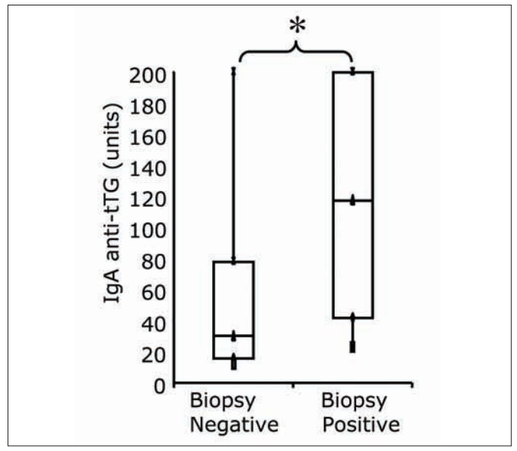


Figure 1: Relationship between small biopsy findings and levels of IgA anti-tTG antibodies.

A small bowel biopsy was performed in 33 patients with positive IgA anti-tTG antibodies. Antibody levels (expressed as arbitrary units) are presented in "box and whisker" plots according to whether the biopsy findings were consistent with CD (positive; n=16) or were inconsistent with this diagnosis (negative; n=17). Using a 2-tailed Mann-Whitney U-test, differences were significant between the two groups (*p= 0.007).

Discussion

Several research studies have reported the highly specific and sensitive nature of IgA anti-tTG antibody testing for CD (reviewed in references 9 and 10). However, results from research studies do not always translate perfectly to the real life situation, where performance is most appropriately measured by audit.

Our audit has confirmed once again that IgA anti-tTG antibody testing is an excellent screening test for the exclusion of biopsy-proven CD, with a negative predictive value of 100% in this series. Together with several additional studies[9, 10], this means that a diagnosis of CD is highly unlikely if testing yields a negative result. The rare situation in which complete IgA deficiency may lead to a false negative result should however be borne in mind.

Nonetheless, our audit has highlighted two findings which may represent causes for concern. First, we identified a high frequency of false positive results when patients are screened for CD by measurement of IgA anti-tTG antibodies. In earlier studies, problems were identified in the performance characteristics of assays that used purified guinea pig derived tTG as the antigen source[14]. However, even with recombinant human tTG (as used here), half of the abnormal results identified were in fact false positives. Similar findings have been reported in some recent research studies[15-17]. A possible solution to this problem may be to confirm positive results using the more stringent IgA anti-endomysium antibody test. However, further research followed by local audit will be required to validate this approach.

The data from our audit also present a second disturbing question – namely that we, as doctors, are not terribly good at identifying patients who need to be screened for CD. Given that the baseline prevalence of CD is about 1% in the UK population[1], it is noteworthy that testing by general practitioners and paediatricians yielded a rate of positive testing for IgA anti-tTG antibodies that is only marginally greater than that expected by whole population screening. Even in patients whose symptoms mandated referral to a gastroenterology service, the test "hit rate" was less than 5%. These findings are even more concerning when we consider that only half of those patients in whom we identified IgA anti-tTG antibodies ultimately proved to have biopsy confirmed CD. Together, these data serve to reinforce how difficult it can be to identify this common clinical condition whose protean and subtle manifestations frequently hinder diagnosis.

Summary

- Serological testing for coeliac disease most commonly involves the measurement of IgA anti-tTG antibodies.
- Many research studies have indicated that the specificity and sensitivity of such testing for CD is very high in both adults and children.
- This audit emphasises the need for local investigation to examine how screening tests perform in real life situations.
- A negative test for IgA anti-tTG antibodies effectively excludes CD, with the rare exception where IgA deficiency renders the test invalid.
- A positive test for IgA anti-tTG antibodies presents a more complex situation since false positives are at least as common as true positives in our experience.

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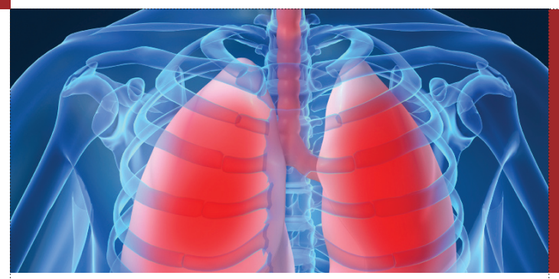
TREATMENT OF ANAPHYLAXIS: CASE BASED DISCUSSION

Hannah R Brown and Michael Vassallo



Anaphylaxis is defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction which is mediated by IgE. It is a life-threatening condition compromising a patient's airway, breathing and circulation.
Patient Management.

Case

You are called to see a 28-year-old man on the medical admissions unit. He is a type 1 diabetic in hospital with a community acquired pneumonia. The nurse tells you that he is looking increasingly unwell and has just been given IV amoxicillin as treatment for the pneumonia. He is not known to have any drug allergies but has not had amoxicillin before. You advise that the antibiotics are stopped immediately and you assess Mr D. On arrival, Mr D does not look well – he is having difficulty speaking to you and appears slightly confused. His respiratory rate is 25 breaths/minute and oxygen saturations are 85% on air. Examination of his chest demonstrates a marked wheeze throughout. Further examination shows him to have cool peripheries and you record a blood pressure of 80/55 and feel a weak, thready pulse, rate 124bpm. His capillary refill time is 3 seconds and he is becoming increasingly drowsy during your assessment. You suspect a diagnosis of anaphylaxis to the IV amoxicillin. How should you manage this patient?

What Is Anaphylaxis?

Anaphylaxis is defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction[1] which is mediated by IgE. It is a life-threatening condition compromising a patient's airway, breathing and circulation. It is estimated to affect 1 in 10,000 individuals per year[2] and results in 20 deaths per year[3].

Recognition Of Anaphylaxis

It is vital to recognise the signs and symptoms early as early recognition and treatment is life saving. Reactions to allergens typically occur rapidly after exposure to the precipitant factor, whether this is a drug, food or other precipitant. Some of the common causes include:

- Foods (such as nuts, shellfish, eggs, milk, soy, wheat)
- Drugs (e.g. penicillins, aspirin, NSAIDs, contrast media used in the radiology setting, blood products and muscle relaxants)
- Stings (including wasp and bee stings)
- Others (including latex, many other foods and drugs)

A history of rapid onset of symtoms over a matter of minutes, compromising the patient's airway, breathing or circulation, combined with skin changes are highly suggestive of anaphylaxis[4]. These criteria combined with exposure to a known allergen, as described by the Resuscitation Council (UK), make a diagnosis of anaphylaxis likely.

Other diagnoses which should be considered include airway obstruction from acute asthma, bacterial epiglotittis or a foreign body, angioedema, shock, vasovagal syncope and panic attacks.

Clinical Features

History and examination is essential to the diagnosis. The following signs and symptoms may be seen:

- Itching
- Erythema +/- Urticaria
- Oedema (including laryngeal)
- Wheeze
- Palpitations/cardiac arrhythmias
- Stridor
- Hypotension (systolic blood pressure <90mmHg)

Treatment

Anaphylaxis is a medical emergency and the principles of airway, breathing and circulation should be applied. Patients should be treated according to the ABCDE approach in the Resuscitation Council's recent guidance: Emergency treatment of anaphylactic reactions[4], see Figure 1. High flow oxygen (15 litres via a non-rebreathing mask) should be given to all patients and rapid fluid resuscitation with crystalloids is required.

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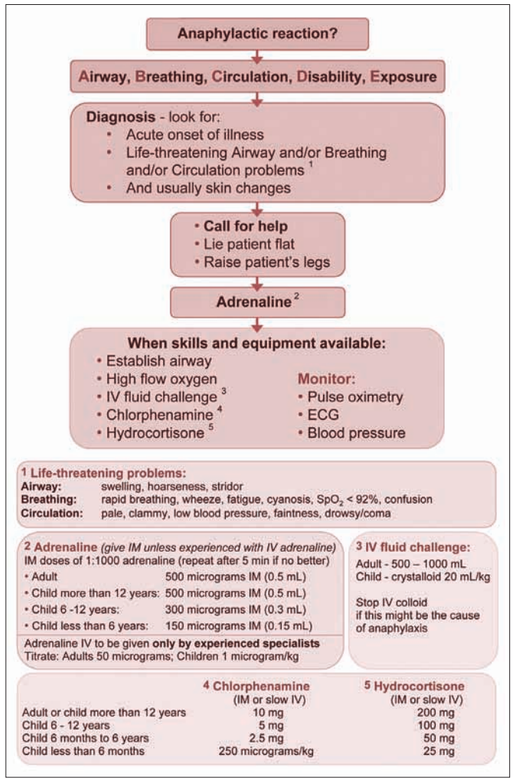

Figure 1 - Anaphylaxis Algorithm.

Rapid administration of intramuscular adrenaline is the priority in anaphylaxis with respiratory difficulties or hypotension[5]. Delays in administration are associated with poor outcomes[6]. In cases of severe anaphylaxis the following drugs should be administered[7]:

- Adrenaline 500micrograms IM (0.5mls of 1 in 1000)
- Chlorphenamine 10–20mg slow IV injection[8]
- Hydrocortisone 100–300mg IV
  (prevents delayed deterioration in severely affected patients)

Adrenaline (Epinephrine)

Adrenaline is the definitive treatment and its α receptor agonist effects reverse peripheral vasodilation and reduces oedema. Its β receptor agonist activity results in bronchial dilatation, enhances myocardial contractility and inhibits activation of mast cells linked to IgE mediated allergic reactions[9]. Further effects suppress histamine and leukotriene release. Adrenaline should be given intramuscularly into the anterolateral thigh. The subcutaneous route has a much lower absorption[10] and is therefore not preferred.

Intravenous adrenaline is a much less safe route of administration and can be associated with significant hypertension and cardiac arrhythmias, as just a few of the side effects[7]. Its use is recommended with extreme caution by specialist staff only where full monitoring of the patient, including cardiac monitoring is available[4,7]. It is also worth noting that in this scenario the 1 in 10,000 preparation is used and not the 1 in 1000 preparation, which is used IM.

If there are signs of wheeze then nebulised salbutamol should be given. If cardiac arrest occurs then cardiopulmonary resuscitation should be started[11] and the use of IM adrenaline should be abandoned.

For any patient with anaphylaxis, obvious precipitant factors should be removed or stopped. In hospital, this may be intravenous drugs such as penicillins or colloid fluids.

Post-Acute Care

Following anaphylaxis patients should be observed in hospital for at least 6 hours to ensure any late reactions are monitored and treated appropriately[12]. The measurement of mast cell tryptase levels is a specific test which assists in the diagnosis of anaphylaxis. The degranulation of mast cells in anaphylaxis results in a detectable rise in blood tryptase concentration between 30 minutes and 6 hours after the onset of symptoms, usually peaking 1–2 hours after the onset of symptoms. Ideally three samples of blood should be obtained, the first once initial resuscitation measures are underway, the second at 1–2 hours and the third sample after 24 hours to provide a baseline measurement.

Referral should be made to a clinical immunologist for follow-up of these investigations. This enables identification of the triggering factor(s) through skin testing and education of patients and their families in avoidance of allergens. It also allows for the provision of pre-loaded auto-injector adrenaline syringes for use in an emergency and instruction on their use. For children this may need to involve their school.

Conclusion

Research has shown few junior doctors are adequately prepared to identify and treat anaphylaxis[13]. While most junior doctors correctly identify the drug required in this emergency, some incorrectly identify the best route of administration and further confusion exists surrounding the correct dose[14] which differs from cardiac arrest.

Suggestions have already been made for prefilled syringes to be kept on all crash trolleys labelled for use intramuscularly in anaphylaxis[13,14]. This is one step which, combined with training to improve recognition and treatment, will help junior doctors safely manage acute anaphylaxis.

The same principles apply to treating children with anaphylaxis, although the doses discussed in this article refers to the management of adults.

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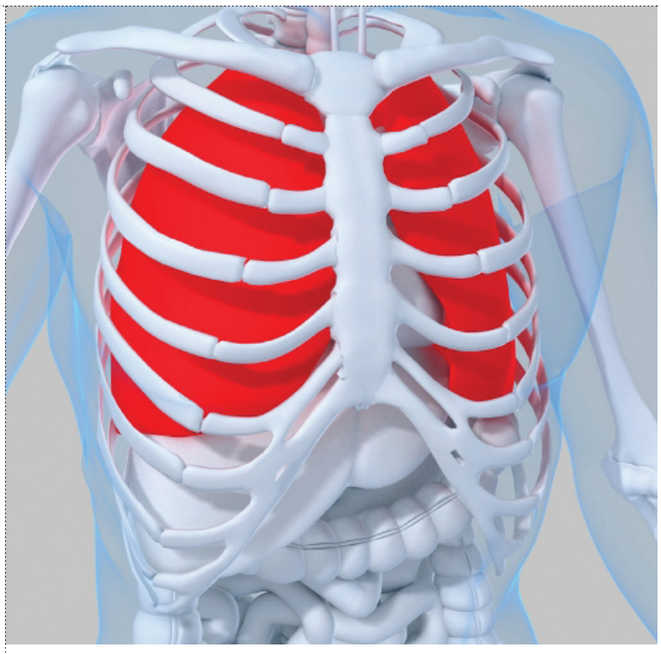

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URTICARIA AND ANGIOEDEMA

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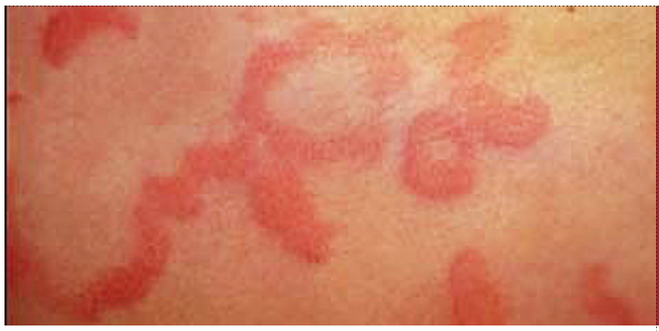

Urticaria describes short-lived slightly raised, itchy red patches anywhere on the body.
Patient Management.

Introduction

Urticaria describes short-lived slightly raised, itchy red patches anywhere on the body. Angioedema describes swelling occurring slightly deeper in the skin and mucous membranes. Urticaria may affect more than 20–25% of the population at some point in their lives. Most patients suffer both urticaria and angioedema although one may predominate in some patients. Urticarial patches are often pale in the centre and vary between a few millimetres across to 10cm or more across. These patches can sometimes become confluent giving the impression of diffusely swollen, itchy red skin. They can affect any area of the body and usually last from 30 minutes to as long as 48 hours or more. Apart from the discomfort of the itching, systemic symptoms are usually absent in simple urticaria and angioedema. Some patients may feel tired. When the individual patches of urticaria last longer than 36 hours, or are associated with bruising, then an inflammation of cutaneous blood vessels should be suspected as part of a cutaneous vasculitis. The latter is often associated with arthralgia, myalgia and mild fever.

Pathophysiology

The erythema, itching and swelling evident in urticaria is caused by the activation of mast cells either by antigen cross-linking cell surface antigen specific IgE antibodies or possibly by anti-IgE auto-antibodies. In some cases there may be direct mediator release by unmyelinated nerve terminals or activation of the kinin system. Histamine appears to be the principal mediator involved in the early phase response while others (such as leukotrienes and prostaglandins) are produced in the late-phase response via arachidonic acid metabolism. Several other mediators (such as complement proteins, neuropeptides, platelet activating factor, kinins and various chemokines) have varying importance in the different types of urticaria and angioedema. Histologically there is dilation of small venules and capillaries, flattening of rete pegs and swelling of collagen fibres. The multitude of mediators involved explains why urticaria is sometimes poorly responsive to antihistamines alone. The ability of the unmyelinated nerves to directly release some of the mediators may explain why urticaria is sometimes precipitated by and often aggravated by stress and changes in mood.

Aetiology Of Urticaria

When trying to determine the cause of the urticaria and angioedema, it is initially important to separate an acute from chronic urticaria by noting the frequency of the urticarial reactions and the total duration of the illness. In acute simple urticaria, the episodes are isolated events and may be caused by food allergy, viral infection (which may be subclinical), insect bites/stings or drug reactions (aspirin, NSAIDS, penicillins, etc.). A causal relationship between these factors and the urticaria is often apparent from the history.

In some patients, small discrete patches of urticaria may be evident with heat or exercise and lead to a cholinergic urticaria. In other patients the urticaria may be precipitated by physical factors, such as pressure, cold and sunlight. Dermographism describes urticarial wheals when the skin is scratched. In some instances.

Chronic urticaria (CU) describes of the presence of regular (greater than or equal to 3 per week) urticarial reactions for more than 6 weeks. In the absence of any features of vasculitis these are described as idiopathic. Allergy to specific foods or sensitivity to colourings and preservatives is almost never involved in CU. In some patients there may be an autoimmune basis; a temporary dysregulation of the immune system by a viral infection; sustained stress or strong emotions leading to auto-antibodies directed against the IgE receptor (FCeRI) or against IgE itself with both being capable of causing direct mast cell activation that bypasses the need for the IgE antibody to bind a specific allergen.

In Western countries, worm infestation is rarely a cause of chronic urticaria although it should be considered if the patient has undertaken recent foreign travel. When chronic angioedema occurs in isolation of any urticaria, it is important to exclude drugs as a cause. These include ACE inhibitors, e.g. Enalapril and sometimes SSRIs. If the patient is not taking any such medication, then check if the patient has any infection within the sinuses or teeth and if present treat appropriately. Note that CU may be worsened by the use of ACE inhibitors and NSAIDs and it is worth discontinuing or using alternatives if this is possible. Where angioedema is the sole problem, associated with recurrent abdominal pain, difficulty in breathing and if it occurs in a child or young adult, it is important to check for hereditary angioedema (HAE, see later). While HAE is dominantly inherited, there are cases due to new mutations in the C1 esterase inhibitor gene. It is important to recognise this condition owing to the danger of airway occlusion.

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Where a vasculitic urticaria is suspected, it is important to check for the symptoms and signs of illnesses associated with immune complex deposition and immune dysregulation accompanied by auto-antibody formation. These include systemic connective tissue disorders (such as SLE, chronic infection in the sinuses, lungs, urinary or gastrointestinal tract) for any symptoms suggestive of a lymphoma. Finally try to determine if any factors are perpetuating the urticaria, e.g. stress and frustration or chronic infection such as sinusitis or dental abscess.

It is important to tell patients with CU that a cause may not be found in 70–80% even with the most detailed examination and laboratory investigation. For these patients with idiopathic urticaria a careful diary may help to pinpoint possible triggers. However, patients should be warned not to let this search take over their whole life as this frequently leads to increased stress that may prolong the urticaria.

Investigations

When an allergen is considered of aetiologic importance in acute urticaria, it is important to confirm or exclude this by either skin testing or blood tests that estimate the allergen specific IgE.

- Skin prick testing is rapid and relatively cheap and can utilise either commercial reagents or sometimes fresh fruit, vegetables and certain other foods. It is a remarkably safe procedure although care is required when testing in a patient with suspected anaphylaxis.
- Intradermal skin testing is used for testing for allergy to drugs, insect venom and anaesthetic agents in particular.

For both types of testing, it is important that positive and negative controls are included in the testing procedure. These will check for non-reactivity due to oral antihistamines and certain other drugs (positive control) and non-specific skin reactivity due to dermographism (negative control).

In patients with CU and angioedema, a basic panel of investigations should include the following:

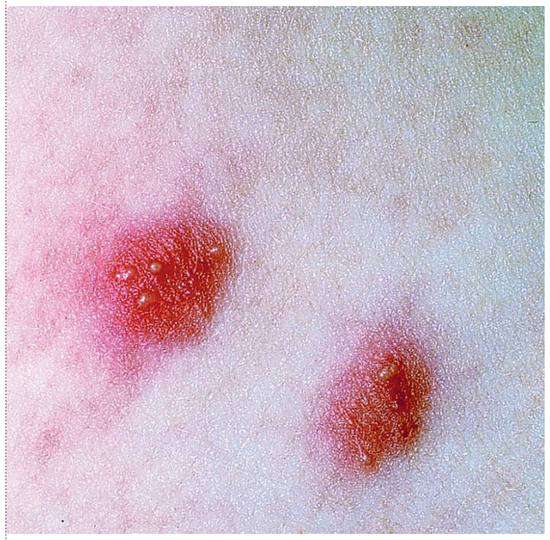
- Full blood count – to check for any lymphoproliferative disease
- ESR – to check for any persistent immune activation from either autoimmunity, infection or lymphoproliferation
- Anti-nuclear antibodies – to check for any underlying connective tissue disorder
- Anti-thyroid antibodies – anti-TPO abs may be found in 10–25% of patients with CU with some having overt hypothyroidism requiring treatment
- Serum immunoglobulins and electroprotein analysis – this is especially important in the elderly and if angioedema is the sole problem as a monoclonal gammopathy of unclear significance or very rarely other lymphoproliferative processes may underlie "acquired angioedema" (AAE).
- Complement C4 assessment is the best way to screen for hereditary angioedema HAE) or indeed acquired angioedema arising from an underlying lymphoproliferative process. Levels that are well within the normal range virtually exclude both. If the C4 level is low then arrange a serum C1 esterase inhibitor analysis. If the latter is low then refer to an immunologist to check for HAE or AAE. Most cases of slightly low C4 in otherwise healthy people are due to one or more C4 null genes.

Other investigations would be based on any clinical symptoms and may include:

- Anti-helicobacter serology for dyspepsia
- Sinus and/or chest X-ray if any evidence of chronic sinusitis or chest infection
- Rheumatoid factor if patient has an inflammatory arthritis

Treatment

The best treatment for urticaria and angioedema is clearly to identify the cause and avoid it. Where this is not possible, the main aim of treatment is to provide symptomatic relief and suppression of the urticarial wheals.



Treatment should commence with a regular non-sedating antihistamine tablet. A short acting sedating antihistamine may be useful if the attacks are nocturnal or if a persistent urticaria disrupts sleep. The vast majority of the newer antihistamines are very safe even in patients with cardiac problems. There are individual variations in efficacy and tolerance. Most patients notice none or few side effects and the therapy may be continued for many years without long-term complications.

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The antihistamines commonly used in the clinic are:

- Cetirizine or Levocetirizine (Xyzal)
- Fexofenadine 180mg (Telfast 180)
- Loratadine or Neoclarityn
- Mizollen (Mizolastine) probably contraindicated in patients with cardiac problems or in patients on macrolides and imidazoles
- Chlorpheniramine (Piriton) may be used in very young children and in pregnancy

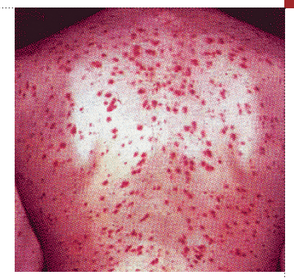
Several different types of antihistamines may need to be tried to see which one works best with the least number of side effects. They often need to be used at doses higher than those used for allergies. Alternatively combining different antihistamines may be worth trying. Sedating antihistamines should be used at night and non-sedating ones for the daytime. It is important to tell patients that antihistamines provide symptomatic relief of their symptoms while waiting for the urticaria to resolve. In some patients the addition of a leukotriene receptor antagonist (such as montelucast) may be worth considering although the evidence that it provides any benefit is very limited.

For acute urticaria a brief course of oral prednisolone therapy may be tried at a dose of 25mg daily for 5 days and reducing by 5mg per 2 days thereafter. Doses of 25mg or less of prednisilone are only rarely associated with psychosis.

When antihistamines used at double the conventional dosage have failed or provided only partial symptomatic relief then an H2 antagonist (such as Famotidine or Ranitidine) may be considered. However, the evidence that these provide benefit is very limited and some consider that they work only by reducing the hepatic degradation of any conventional anti-H1 antihistamine that is being used.

In patients in whom the urticarial patches persist for more than 24 hours or there is bruising evident hydroxychloroquine at 200mg daily should be considered. Before commencing this treatment, it is important to make sure the patient has normal levels of red cell Glucose-6-phosphate dehydrogenase (EDTA blood specimen sent to department of haematology). This would be especially important in Asian, Mediterranean and Afro-Caribbean patients. The patient's near vision should also be checked and the results recorded in the notes as this therapy can in rare cases alter vision. However, this is usually only observed at higher doses used for several years. Patients should be warned that the hydroxychloroquine works slowly and that little benefit may be observed in the first 2–4 weeks. The therapy then increases in effect for a further 4-6 (en dash) months and should be continued for between 6–12 months.

Patients not responding to the above medication may need treatment with dapsone, colchicine and very occasionally with either cyclosporin or intravenous immunoglobulin. These patients should be referred to an Immunology, Dermatology or Allergy Clinic.



Prognosis

Acute simple urticaria and angioedema has a very good prognosis and well over 90% will not have a further attack. In others, the attacks may occur sporadically over a few days, weeks, months or years. However, the tendency in each case would be for a gradual resolution over a period of a few months. It is important to note the trend rather than the severity of an individual episode. Urticaria with varying degrees of angioedema, lasting a few days and not associated with specific foods, is often the result of a viral infection in children and this type only rarely recurs. Clearly acute urticaria and angioedema arising from a specific food or drug allergy will only recur if there is continued or further exposure.

When urticaria becomes chronic with recurrent episodes occurring over at least 3 months, the prognosis becomes less favourable the longer the overall duration of the urticaria. Nevertheless, 60–70% with CU will be entirely free of their attacks by 1 year. The figure is slightly less when the urticaria is accompanied by angioedema and less so at about 30–40% if angioedema occurs without urticaria. Several factors can perpetuate the urticaria when it becomes chronic including the stress and anxiety associated with having a skin condition that can cause cosmetic disfigurement and one which is uncomfortably itchy and highly unpredictable. If the patient can be encouraged to relax and be optimistic that the problem will go, then this frequently encourages a resolution of the problem. In any event, patients should be reassured that simple urticaria, no matter how often it occurs or how long it persists, does not indicate that they have any serious underlying illness. The simple blood tests, mentioned above, will certainly help in emphasising this point.

When urticaria has been brought on by physical stimuli (such as physical pressure, vibration, cold or sunlight) the prognosis is more guarded. In this case, the urticaria tends to resolve in fewer than a quarter of all such patients. Regardless, all patients can be offered symptomatic relief with either regular or intermittent antihistamine therapy. Clearly, all such patients should avoid the physical stimuli that provoke their urticaria. Patients whose urticaria is induced by cold (so-called cold urticaria) deserve special counselling. These patients should be cautioned against swimming or taking a cold bath or shower as collapse and occasional fatalities have occurred from massive histamine release.

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RESEARCH

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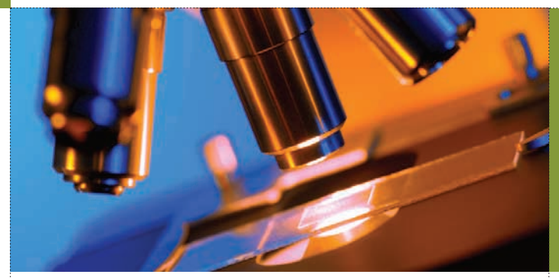

The opportunity to improve things for our patients and advance scientific knowledge is an excellent part of being a health care professional.
Good Medical Practice.

Medicine Depends On Research

Without research, there is no way to demonstrate the best way to treat a particular condition, or the most useful test in a clinical situation. The opportunity to improve things for our patients and advance scientific knowledge is an excellent part of being a health care professional, but conduct in research needs to be of an exceptionally high standard in order to underscore both the integrity of the research itself, and to rightly repay the trust patients place in us when they agree to take part in it. While much scientific research is laboratory-based, this article will focus primarily on the key features of good practice in relation to research with human participants, as that is of most immediate relevance to the clinician. It is not an exhaustive review, but rather a tour of some key concepts and associated organisations and systems that exist to ensure good practice in research.

It is appropriate to start by directing the reader to an authoritative reference on this subject. The General Medical Council document "Research: The Roles and Responsibilities of Doctors" published in 2002, is available on the Council's website[1], and provides a clear benchmark in this area for the UK practitioner. More detailed information is available through Good Clinical Practice (GCP) which is an international quality standard that is provided by the International Conference on Harmonisation (ICH) and is used as a template by regulatory bodies for clinical trials involving human subjects (**http://www.emea.europa.eu/pdfs/human/ich/013595en.pdf**).

Informed Consent

It is essential that any patient entering a research study understands what is being asked of them and what might happen to them. They should be competent to give consent. Research staff often use information leaflets, which should be available to a potential participant as part of the initial discussion. The person can then be left to peruse the information, and after a reasonable time period the research staff can return and answer any questions that arise from it, always seeking to ensure that the person's understanding is complete. The appropriate use of language is an important part of both the verbal and written communication with a potential participant at this stage. Jargon should be avoided and the research proposed should be explained in a straightforward way ensuring that cultural and language issues are addressed. A clear explanation of risks and benefits for the participant is essential in order for the researcher to be confident that the consent the person gives is appropriately informed consent.

There is a tendency to give vast amounts of information when recruiting a participant, but a careful balance needs to be struck between rightly giving information and simply flooding someone with facts they do not need to grapple with. Uncommon exceptions to the need for informed consent in adults do exist, but these occur in very specific circumstances where a research ethics committee may choose to sanction research involving persons who lack the necessary competence to give informed consent (e.g. severely ill patients who are unconscious). It is also important that any research planning takes account of the potential for participants' ability to consent to change: they might, for example, be intubated on an intensive care unit as part of their illness. It is important that they understand what will or will not happen in that circumstance if they have agreed to take part in a research study. They should also understand how to withdraw from participation should they wish to at any stage.

RESEARCH

Matthew Welberry Smith

Confidentiality And Data Storage

Any research involves the collection of information over and above (or in parallel to) that collected for routine clinical care. There is more than one way of collecting the information; it may be fully anonymised or linked anonymised. (The latter refers to the alignment of information with specific patient names, but this can only be done with a decoding key and will usually be done by the principal investigator.) Alternatively data may not be anonymised at all. Secure storage of such data is essential, and goes further than simple password protecting of files. The servers and hard drives where the information is stored need to be secured both physically and in terms of any intranet network they are connected to. Research ethics committees now routinely ask about data storage and any expected use of portable data systems (such as laptops or USB drives). Appropriate steps must be taken to ensure any data in portable form is not at risk of being stolen or misused. This can be addressed by encryption of portable devices. Great care must be taken when considering communication about research over email. If in doubt about whether an electronic medium is secure with respect to data transfer, it is wiser to find an alternative than take a risk with it. Sometimes anonymous samples have the potential to be used in future, as yet unplanned, research and if so specific consent for this should be sought, and arrangements for longer term secure data storage need to be in place. Obviously publication of research results should not contain any patient identifiers.

Ethical Approval

The majority of research (excluding some statutory public health surveillance) requires the approval of a Research Ethics Committee. There is now an online Integrated Research Application System[2]. Applications for ethical approval have to cover a vast range of possible ethical issues, and as a result can seem complex and long, but serve an important purpose in ensuring a research study has been thoroughly thought through. For the new researcher, advice from more experienced colleagues, who have been through the process in the past, can be invaluable.

Research And Development Approval

Research and Development departments of individual NHS institutions involved in any research need to give approval before the research can be carried out on a site under their auspices. This process has been carried out in conjunction with the central process for obtaining Research Ethics Committee approval, but will be brought under the control of the National Institute for Health Research in their Coordinated System for gaining NHS research Permission (known as NIHR CSP)[3], which went live mid-November 2008. Again, for the new researcher, advice from more experienced colleagues, who have been through the process in the past, can be invaluable.

Registering Clinical Trials

As an aspect of the openness and transparency now expected of research, the majority of trials are registered on one of several databases, such as Current Controlled Trials **(www.controlled-trials.com).** The British Medical Association website has a useful summary of regulations related to Clinical Trials in the UK, with helpful links to a number of trial databases[4]. The UK Clinical Trials Network (UKCRN)[5] is building a complete picture of clinical trials across the UK and aims to develop and strengthen the NHS infrastructure to support the delivery of UK clinical research. Many journals now demand registration of a trial on a recognised open access database before they will consider publication of material arising from the work. The registration should be performed at the start of the process, however, not retrospectively when publication becomes a possibility!

Intellectual Property

Most major research funding organisations, and UK academic institutions, will stipulate how any intellectual property arising from research undertaken in their departments will be handled. Intellectual property is of major importance not only for appropriate recognition of interested parties in any future developments from the work, but also as part of ensuring that discoveries from research are fully exploited. Having a framework in place to enable research findings to move rapidly forward is vital as part of the infrastructure to ensure translation of research into practice.

Conflicts Of Interest

Bias can be introduced into research in many ways. Among the most obvious are conflicts of interest arising from specific funding, or involvement in a commercial organisation with an interest in the area under consideration. It is important that in appraising research, the reader has an understanding of these potential biases, even though the majority of authors have honourable intentions in striving for objectivity in their work. Conflict of interest statements are now routine in almost all forms of publication (even editorials), and are part of good practice. Look at the end of this article for my own example.

Funding

Funding for research is available from many different sources. Some funders focus on specific diseases, or specific types of scientific work. Research may be funded by industry or by pharmaceutical companies, and partial funding collaborations with these bodies also exist in many forms. There is no problem with the involvement of such collaborators provided appropriate acknowledgement of conflicts of interest are made when findings are made public. It is in the interest of commercial organisations for researchers to be open about this, so that it is evident that every effort has been made, in a good research study, not to bias the results one way or another.

However a study is funded, getting the funding set up can be a major obstacle for the new researcher. Funders naturally want extensive information before they commit to payment, and so detailed paperwork is usually essential even to apply. The curriculum vitae of a potential researcher will be scrutinised in detail.

RESEARCH

Matthew Welberry Smith

Plagiarism

The presentation of another persons work as if it were your own constitutes plagiarism. It is a serious offence, and not to be taken lightly. It can never be considered acceptable practice, and is inappropriate to the probity expected of researchers. Failure to acknowledge sources, even accidentally, can be seen as plagiarism. Anyone producing a publication should fully acknowledge the sources they have used.

Data "Manufacture"

There have been high profile cases regarding the use of data manufacture. This describes the fabrication of results, an example being the Korean scientist Hwang Woo-suk's work on cloning[6]. Obviously this is entirely contrary to good research practice. The pressure to produce good results should never lead a researcher to falsify or inaccurately present their data. It is much better practice to publish an important negative finding (despite the difficulties of publication bias) than succumb to dishonesty in this way.

The UK Research Integrity Office

The UK Research Integrity Office (UKRIO) is an independent body launched in 2006 which offers advice and guidance to universities and other research organisations, and also to individual researchers, about the conduct of research. The aims of the organisation are to promote the good governance, management and conduct of research and share good practice on how to address misconduct in research, as well as giving advice and guidance on specific cases. Further information is available on their website[7].

Life As A Researcher

If you have read this far, you may feel like research is drowning in a sea of regulation and requirements, with multiple organisations in existence that you had never heard of before, and that a damper has been put on your laudable research aspirations. So to lighten the tone, let me tell you how immensely enjoyable research can be. There is little to compare with the knowledge that you have discovered something, even if that something is a small piece in the greater puzzle of medical knowledge in that area. Furthermore, most people involved in research really care about what they are doing, and this makes for a stimulating environment, with an emphasis on teamwork, since little can be achieved by one person alone with their experiment! Dedication is required in research, and it is by no means the easy ride it may once have been wrongly portrayed as. It is now appropriately underpinned by regulation. Good practice in research leads to the best research, and the best research leads to better patient care. Keep that vision in mind and see the necessary paperwork as a framework for your aspirations.

In summary, good research practice involves the high standards that should be part of every doctor's professional life, applied in ways that are different to clinical practice, but just as important. There are an array of helpful organisations and websites to facilitate this practice in the UK, and it is worth gaining access to these before embarking on a project. Key to all research involving patients is an underlying respect and gratitude for their willingness to forge new paths in medicine with us, despite the risks that can involve. Ensuring that patients are informed and their care is as safe as possible is central to research; as is respect for the privacy of any data related to them. They must be reassured that any results obtained will be published honestly and that we the researchers will conduct the research transparently with appropriate reference to regulatory organisations. We must remember to thank them publicly no matter how the research progresses as it cannot happen without them.

My very own conflict of interest statement: Matthew Welberry Smith is currently involved in laboratory-based translational research on biomarkers in renal transplantation, funded by the Medical Research Council, Kidney Research UK, the Yorkshire Kidney Research Fund and the Leeds Teaching Hospitals Charitable Foundation. As a result he will probably have overstated the complexity of the research world, in order to impress you, and exaggerated the fun involved in order to persuade you to join him in the world of research. *Read with caution.*

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CAREERS FOCUS: WORKING AS A ROYAL NAVAL DOCTOR

AM Wood and IM Wood

Many doctors do not know what opportunities and experiences are available in the UK Armed Forces, or how to apply for a commission in the armed forces. Each of the three services are different and anyone looking at a career in the armed forces would be advised to investigate the career opportunities in at least two of the forces, before making a decision.
Teaching & Training.

Introduction

Having finished medical school and starting work as a FY1 doctor and experiencing life as an NHS doctor for the first time, many people start to think about what specialty they want to do. Despite the "walk-back" from run-through training occasioned by the "decoupling" process, there may still be less flexibility and opportunity to gain general medical experience before settling on a definitive career pathway than was possible in previous years.

While some doctors look towards Australia and New Zealand for experiences outside the NHS (a few volunteer for charities like Operation Raleigh and other Expedition Medicine organisations), many doctors consider joining the UK Armed Forces for either a short service commission or for a full career.

Many doctors do not know what opportunities and experiences are available in the UK Armed Forces, or how to apply for a commission in the armed forces. Each of the three services are different and anyone looking at a career in the armed forces would be advised to investigate the career opportunities in at least two of the forces, before making a decision.

How Do You Get Started?

During your medical school and Foundation Years you will have the opportunity to attend many careers fairs, at many of these the Royal Navy recruiters will be present and this is the easiest way to make contact. If you prefer a more direct route you could contact the RN recruiters directly on 0845 607 5555 or via the Armed Forces Careers centre on most town high streets.

Once you have made contact with the Royal Naval Medical Services, you will be sent a questionnaire about yourself and invited to attend a 3-day acquaint with the Royal Navy in Portsmouth and Gosport. This is as much for you to find out about the Royal Navy and meet Royal Naval Doctors as it is for them to find out about you. After this you can have the opportunity to have acquaint visits to other units in the Royal Navy, however, these are done on an individual basis.

After your Royal Naval acquaint visit, you will be invited to apply for the Admiralty Interview Board (AIB). This is an interview board that all Royal Navy and Royal Marines officers have to take, regardless of branch. It is conducted over 3 days and is designed to test you physically and mentally to assess whether you possess the qualities required for an officer in the Royal Navy. Before you arrive you will be sent a questionnaire about yourself, which must be filled in and submitted before you attend the interview.

During the AIB you will sit a number of tests: a test in verbal and non-verbal reasoning; a test in numerical fluency, reasoning and statistics; a mental agility and spatial orientation test; a general knowledge test about the Royal Navy; and an essay aimed at assessing your written communication skills.

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You will also have to participate in a multistage fitness test, also known as a bleep test; a practical leadership task; and tabletop planning exercises. These tests are designed to test your fitness level, leadership and teamwork skills. The final part of the interview will be a competency-based interview. If you meet the standards required of the AIB you will be invited to attend a medical on the same day. Once all applicants have taken the AIB, they are placed in order of merit and a final selection is made.

Starting Training

The first 6 months of training starts in the September after being accepted into the Royal Navy. Training takes place around Portsmouth and Dartmouth. During the New Entry Medical Officer training you will:

- Conduct Basic Leadership and Naval Officer training at Britannia Royal Naval College, Dartmouth for 8 weeks
- Attend a Battle Field Advanced Life Support course and other trauma and medical courses to equip you with the skills required to work around the globe
- Attend diving medicine and flying medicine courses
- Attend several occupational specific courses to enable you to conduct medicals and assess Royal Naval personnel
- Attend a Tropical Medicine course
- Attend a Basic Sea Survival course

On completion of this 6-month training period you will be ready to deploy with any of Her Majesty's Ships or Submarines around the world or prepare to deploy on operations with the Royal Marines or other elements of HM Armed Forces.

General Duties

After finishing the New Entry Medical Officer course, post-Foundation Year Medical Officers work for 2–3 years undertaking their general duties in different areas of the Royal Navy. In broad categories these are: the Surface Fleet, the Royal Marines and the Submarine Service. In addition, appointments are available in Shore Establishments and Naval Air Stations. This general duties period gives the Medical Officer the broadening skills and experience required of a Service Medical Officer, or, for those who leave after this stage, life, leadership and medical experiences that they can apply to their careers working for the NHS or general practice.

The Surface Fleet

Royal Naval Medical Officers on board HM Ships travel the world looking after their crew of 150–300 personnel. The diversity of experiences is immense and can be as varied as travelling to the Far East on diplomatic missions, to anti-piracy campaigns west of Africa. The West Indies Guard Ship is frequently involved in hurricane relief efforts and anti-drug smuggling operations. Deployments can be as long as 6–7 months with many port visits in that time. Operationally the fleet always has a presence in the north of the Arabian Gulf and other operations around the world ensuring security on the world's waterways, in which the Medical Officer will be fully involved in the planning and conduct of operations.

The Royal Marines

After passing the Royal Marines Commando course and earning the coveted Green Beret, Medical Officers can deploy with Commando units or other Royal Marines units to conduct training and operations throughout the globe. Within a 2-year attachment to a Commando unit, a Medical Officer would normally conduct one Arctic Warfare training exercise in either Norway or the United States and may conduct Jungle training in Belize or Amphibious training in the Mediterranean or elsewhere. At the moment most Commando units would also deploy to Afghanistan or another Operational area where the Medical Officers would get first-hand experience of dealing with patients in difficult situations.

The Submarine Service

After New Entry training, Medical Officers who want to work with the Submarine service will conduct a further 6 months of submarine-specific training to qualify them to work on a submarine. Submarine Medical Officers become an integral part of the submarine's team, and most work on the nuclear submarines that provide the UK's nuclear deterrent. Some Medical Officers work on the smaller Trafalgar class attack submarines, which deploy around the world and visit many ports flying the flag for the UK.

Shore Establishments And Naval Air Stations

Some Medical Officers will be attached to the Fleet Air Arm while they are in the UK and at times abroad, providing medical support for the aircrew while training and deployed on operations. In the UK there are some opportunities to become involved with the Air Sea Rescue Service out of Culdrose Naval Base and also with the RAF 22 Squadron based near Barnstaple, Devon. On top of this there are opportunites to supervise submarine escape training and Royal Naval/Royal Marines training at some of the UK bases. There is also a requirement for Medical Officers at each of the main base ports, who provide medical cover for RN personel in the UK. Some of these Medical Officers will become involved in the Submarine Parachute Assistance Group, which is a team of specialists available to parachute into the water around the world and assist submarines in difficulty.

Adventurous Training And Sport

Adventurous training and participation in sport is actively encouraged in HM Armed Forces. As well as having the opportunity to participate in these activities as an individual, there is also an ongoing requirement for medical support in order for personnel to take part in these activities. HM Armed Forces, therefore, provide postgraduate training opportunities in conjunction with the University of Wales Institute Cardiff in Sports and Exercise Medicine up to MSc level.

The variety of opportunities available in adventurous training and sport is considerable: for example, in recent times Medical Officers have been diving in the Ascension Islands, climbing Mount Everest, skiing to the North Pole, and playing sports ranging from water-polo, netball and rugby in countries as far apart as Australia, Canada and the Caribbean.

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Postgraduate Training

During their last year of general duties, it is normal for Medical Officers to apply to start specialty training. Postgraduate training is run by the Defence Postgraduate Medical Deanery (DPMD) based in Birmingham. The interview and selection process for entry into training posts is run in conjunction with the West Midlands Deanery to ensure that applicants meet the person specification for entry into training in the relevant specialty.

The Defence Medical Services, on behalf of the Royal Navy, oversees the training of Medical Officers in secondary care specialties to ensure that consultants are of equal standing with their NHS colleagues in regard to qualification, experience and personal qualities. The Defence Medical Services follow the training required for NHS trainees as closely as possible, while also ensuring that the needs of the Royal Navy and other services are met.

Currently CT and ST training occurs in the regions to which the five Ministry of Defence Hospital Units (MDHUs) are attached and the Royal Centre for Defence Medicine (RCDM) and South East Scotland Deanery. This means that military Medical Officers can currently be trained in the following deaneries, dependant on specialty and availability.

- East Midlands Deanery (MDHU Peterborough)
- KSS Deanery (MDHU Frimley)
- Northern Deanery (MDHU Northallerton)
- South East Scotland Deanery (no attached MDHU)
- South West Peninsula Deanery (MDHU Derriford)
- Wessex Deanery (MDHU Portsmouth)
- West Midlands Deanery (RCDM Birmingham)

As well as offering the opportunity to train as a general practitioner, or occupational medicine consultant, the Defence Medical Services require the following specialties of Secondary Care Consultants although not all are required by the Royal Navy specifically:

- Anaesthetics
- Burns and plastics
- Dermatology
- Emergency medicine
- General medicine
- General surgery
- Genito-urinary medicine
- Intensive care consultants
- Maxillary-facial
- Neurology
- Obstetrics and gynaecology
- Ophthalmology
- Orthopaedic surgery
- Otorhinolaryngology (ORL)
- Pathology
- Psychiatry
- Radiology
- Rheumatology and rehabilitation

As previously mentioned, selection is carried out in conjunction with the West Midlands Deanery. Some specialties within the Royal Naval Medical Service are nearly fully manned so entry is very competitive, even for those that have benchmarked successfully.

During the course of CT and ST training some trainees can expect to be deployed for short periods of time to Operational Theatres (such as Afghanistan and Iraq), in order to gain experience in the management of patients who have sustained injuries secondary to military operations. These deployments are constantly reviewed by the Defence Medical Deanery in conjunction with the Royal Colleges and PMETB to ensure that, if they are to count towards training, they meet the appropriate standards required.

Research And Higher Degrees

Research and higher degrees remain as important for Royal Naval and Defence Medical Service specialists as they are for NHS specialists. There are opportunities for trainees to perform clinically-based research in NHS hospitals and attached to universities, as well as conducting it in the Defence Science and Technology Laboratory (DSTL) at Porton Down.

Royal Naval doctors can apply to initiate their own projects and seek funding from the Royal Navy and Defence Medical Services, they are able to use these projects as part of the submission for a higher degree.

Rates Of Pay

In 2008, the salary for a Foundation Year 1 doctor was £39,534 per annum, rising to with RN £52,225 in FY2 and then to £58,164–£71,772 during the first 5-years' post-registration service. Following this, salaries range from £62,819– £94,593 for non-accredited doctors; £94,839–£120,570 for general practitioners; and £75,156–£129,228 for consultants[4].

There are a number of different allowances available to doctors who have to live in rented accommodation and for doctors working on submarines, ships or away from home for extended periods of time. For consultants there is also the possibility of gaining distinction awards of up to £59,576. Currently the pension offered is a non-contributable final salary scheme.

On Completion Of Postgraduate Medical Training

When Royal Naval Medical Officers have completed their training as general practitioners or secondary care consultants there are a number of different pathways available. General practitioners will tend to work for a few years in Naval and Royal Marines bases around the UK looking after serving personnel. There will also be the opportunity to deploy with the Royal Marines and some of the capital ships (aircraft carriers and amphibious ships) around the world, acting as the principle Medical Officer, looking after personnel and managing any emergencies, natural disasters or operational situations that may occur.

There is also the opportunity for Medical Officers to become involved with the command structure of the Royal Navy and Defence Medical Services, either managing medical matters in the fleet and the military as a whole, or becoming involved in the research and training relevant to the military as either a postgraduate dean, senior lecturer or professor.

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Secondary care consultants tend to work within NHS trusts for about 60–75% of their time, with the other 25–40% of their time being employed on tasks directly for the Royal Navy and Defence medicine. Currently consultants are deployed about once a year to operational areas for about 6 weeks at a time, where they will be involved in the management of battle casualties and other injured personnel.

Conclusion

The Royal Navy offers a hugely exciting and considerably varied alternative to working in the NHS. During the early years Medical Officers will enjoy a number of different experiences, to which their NHS counterparts will not be exposed. At that stage some doctors will then leave the Royal Navy and return to the NHS, on completion of a short service commission.

If the Medical Officer volunteers and is selected to remain in the Royal Navy on a longer commission, there is a well-supported postgraduate training process which offers them the opportunity to gain higher degrees; overseas fellowships and continued experiences in operations around the world.

On completion of their training, Medical Officers will continue to be able to work as consultants or general practitioners, combining the opportunities within the Royal Navy with their continued practice working with the NHS.

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WORK-BASED LEARNING, POSTGRADUATE CERTIFICATE AND FY2 GENERIC SKILLS PROGRAMME; AN EFFECTIVE SYNERGY

Ian Donaldson, Jane Reid, Michael Vassallo and Tim Battcock

A feature of all professional practice is that as the newly qualified professional enters into the first period following professional registration they commence what is often described as a steep learning curve while making the transition from being a medical student to a doctor. Teaching & Training.

Introduction

This article describes an innovative educational development and partnership between a Higher Education Institution (HEI) and Foundation Programme Directors/Clinical Tutors from NHS Trusts. One of the first aims of this partnership was to develop a generic skills curriculum to deliver the Foundation programme through a series of jointly delivered study days. After 2 years of successful delivery of the generic skills study days, the initiative was taken to the next stage of developing a postgraduate certificate. This paper sets out the pedagogical background to the postgraduate certificate and explores some of the emerging issues to inform ongoing medical educational methodology, associated learning from other disciplines and essential critique, to inform improvement.

The postgraduate certificate has benefited from an initial intake of FY2s and the initiative will benefit from a Deanery funded evaluation regarding the "FY2 experience" and relationship to the generic skills days.

A feature of all professional practice is that as the newly qualified professional enters into the first period following professional registration they commence what is often described as a steep learning curve while making the transition from being a medical student to a doctor. What is interesting to note is that the wider literature on this subject consistently notes that significant learning takes place during this period of transition while the individual is in work and stimulated by day to day challenges and through learning from and with others in their workplace[1, 2]. The course team of University Faculty and Foundation Programme Directors/Clinical Tutors, felt that the FY1/FY2 programme and MMC agenda more generally provided an ideal opportunity to offer a route to academically credit this learning, which is undertaken and often goes unrecognised, and create routes to future postgraduate study. It was also felt to be useful to provide a structure in which the trainees could effectively reflect upon their development in order to recognise and capture the learning undertaken that would assist them in their future careers both personally and professionally[3]. It was also felt to be a proactive and innovative move, reflective of the anticipated changes in postgraduate medical education. From these drivers the plans for the postgraduate certificate emerged and were approved in September 2007.

To our knowledge, no other Deanery in England has yet taken this step of linking the Foundation programme to an academic award. A decision was made quite early on in the development, not to make the postgraduate certificate compulsory. There was recognition as with other professional groups that making a post qualification award compulsory would enter into complex territory of fitness for practice and professional regulation. Therefore, while completion of the Foundation programme is required for all trainees the postgraduate certificate is optional and seen as potential value added. In the first year of the programme (2007 intake) from a potential pool of 70 FY2 trainees, 29 expressed interest in the programme and 17 enrolled. Some saw the perceived benefit of holding a postgraduate certificate would have on their CV, others saw the value of developing further academic skills, particularly the attainment of a masters degree. The units within the programme are described in Table 1 and were designed to complement the Foundation programme aims of developing a judgement safe, patient-focused and accountable doctor who is ready to move into specialist training. Of significance was the supportive view of the Medical Directors and Chief Executives as to the potential of the postgraduate certificate to facilitate recruitment.

The pedagogical base for this development is work-based learning (WBL). Boud and Solomon[4] note a number of characteristics of WBL that were particularly attractive to the team (see Table 2) and note that the pedagogical approach used has a significant part to play in the development of learning in higher education, including learning at postgraduate level. Over the last decade considerable interest has grown around the value and use of work-based learning in health care[5]. Work-based learning can be described as a:

"... mechanism for learning for work, at work and through work where successful assessment leads to academic credit"[6].

WORK-BASED LEARNING, POSTGRADUATE CERTIFICATE AND FY2 GENERIC SKILLS PROGRAMME; AN EFFECTIVE SYNERGY

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The challenge for the development team was to design a programme with learning outcomes which were sufficiently flexible to cover the wide range of learning experiences, bearing in mind trainees were working in clinically diverse areas, and to devise an assessment strategy that would meet the quality control required for a postgraduate academic programme yet fit alongside the work and learning which the trainees would be undertaking as part of the Foundation programme curriculum. The key to this was the Foundation Programme Directors and Clinical Tutors involvement in the curriculum planning and the actual assessments[7]. A further challenge was to design a programme which fosters learning as an increase in understanding and commitment to medical professionalism, as opposed to an increase in knowledge. The former gives a greater grasp of meaning with a grasp of underlying principles, an ability to transfer meaning to new situations and initiates a longer lasting change in the individual and is often referred to as "deep" learning as opposed to "surface" learning[8].

WBL, as an educational approach, allows the learner to actively engage in the learning process, identifying personal learning outcomes that acknowledge the challenges they face in their workplace and contribute to deep and reflective learning. Support from Foundation Programme Directors, Clinical Tutors, University Lecturers and formative feedback from FY2 assessments provide the trainee with the sense of direction and purpose to foster active engagement in their learning along with the peer support gained from the action learning group sessions. The postgraduate certificate, therefore, forms the bridge between the acquisition of knowledge and the transformation of the person through using a WBL approach[3, 6].

The postgraduate certificate programme team consists of Foundation Programme Directors and Clinical Tutors who are integral to the Faculty, and University Lecturers who lead the units. In addition, around ten other academics of the HEI faculty are involved in facilitating the generic skills days so providing trainees exposure to interprofessional and varied range of views and later perspectives. See Figure 1 for diagram. On enrolment students have an induction into using the University Library Service, which includes access to ejournals and databases through the University Library system. Students have contact with the university team when they attend the generic skills study days, which are delivered on the university site. During the skills days, which all trainees attend, specific time was identified for those taking the postgraduate certificate to meet with tutorial staff to discuss the unit aims and negotiate their learning agreements. It was judged essential, by those involved, that to maximise the use of time and flexibility, to trainees given the constraints of rotas, that protected time was afforded trainees in order to maximise the educational value of sharing experiences. To achieve this each study day was repeated on three occasions to facilitate attendance and minimise problems with release time. Ongoing tutorial support is provided and accessed via email, telephone tutorials and discussion boards and through the essential role provided by Foundation Programme Directors and Clinical Tutors who are based within participants host trust.

There have been a number of key lessons learned and reflected upon from the first experience, namely that:

- Work-based learning can compliment the current and future expectations of MMC and the postgraduate medical curriculum.
- Of significance and based on initial and early evaluation it is delivering a "rich experience" for trainees and contributing to tangible and positive outcomes.
- Provides participants with a clear vision of their post graduate learning/ study trajectory alongside their specialty training.
- Participants have commented positively regarding their reflective and analytical potential as regards advancing and developing their individual professionalism in line with PMETB requirements.

In conclusion, the first cohort is approaching completion and formal graduation. The team is intending to evaluate the programme in the imminent future in a more robust manner, with the support and cooperation of the deanery, that takes due account of progression to specialist training. Central to this positive experience has been the successful establishment of effective working relationships between Foundation Programme Directors, Clinical Tutors and academic staff. The joint efforts at presenting and supporting trainees through what for many is a very different educational experience have been crucial to the programme's success. Second, the value of protected days in which the trainees can meet together and allow opportunity for peer and tutorial support on a regular basis has been instrumental in facilitating the students to be able to engage in a level of reflection required for the students to gain the most from their workplaced learning and progress to analytical self-critical professionals.

WORK-BASED LEARNING, POSTGRADUATE CERTIFICATE AND FY2 GENERIC SKILLS PROGRAMME; AN EFFECTIVE SYNERGY

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Units	Description
Unit 1: Evidencing professional learning	In this unit students choose a topic in which they reflect upon the development of their skills and knowledge through the Foundation programme. Students draw upon evidence collected during the Foundation programme to reflect and explore their personal learning journey and the implications for their future professional practice.
Unit 2: Assuring and improving the quality of patient care	Learning around Clinical Governance, Audit and Patient Safety underpins this unit. Students present an audit they have undertaken and are required to write a report outlining the case for change and how that change could be managed and resourced.
Unit 3: Proficiency in clinical practice	In this unit students are assessed through a viva format demonstrating their skills in aspects of independent and autonomous patient management, including the assessment and management of patients, using patient-centred care and evidence-based practice models.

Table 1: Postgraduate Certificate Professional Practice (Medicine).

All assessments are jointly marked by Foundation Programme Directors or Clinical Tutors and university staff.

Number	Work-based Learning Programmes
1.	Partnership between HEI and external organisation.
2.	Learners are employees within the external organisation.
3.	Programme is derived from the needs of the workplace and of the learner.
4.	Individuals commence at different starting points.
5.	Significant element of learning is around "learning projects" at work.
6.	HEI assess the learning outcomes.

Table 2: Characteristics of work-based learning programmes (Boud and Solomon 2001)[4].

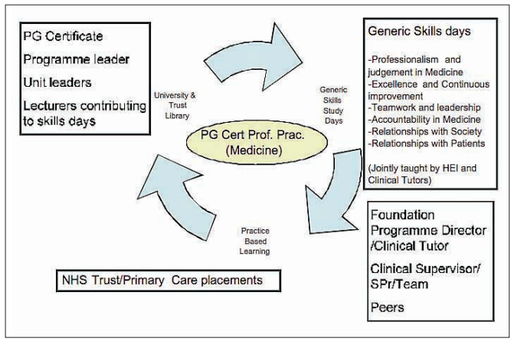

Figure 1: Centre for postgraduate medical research and education.

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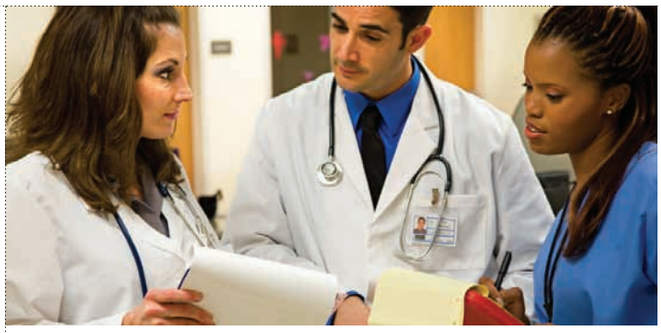

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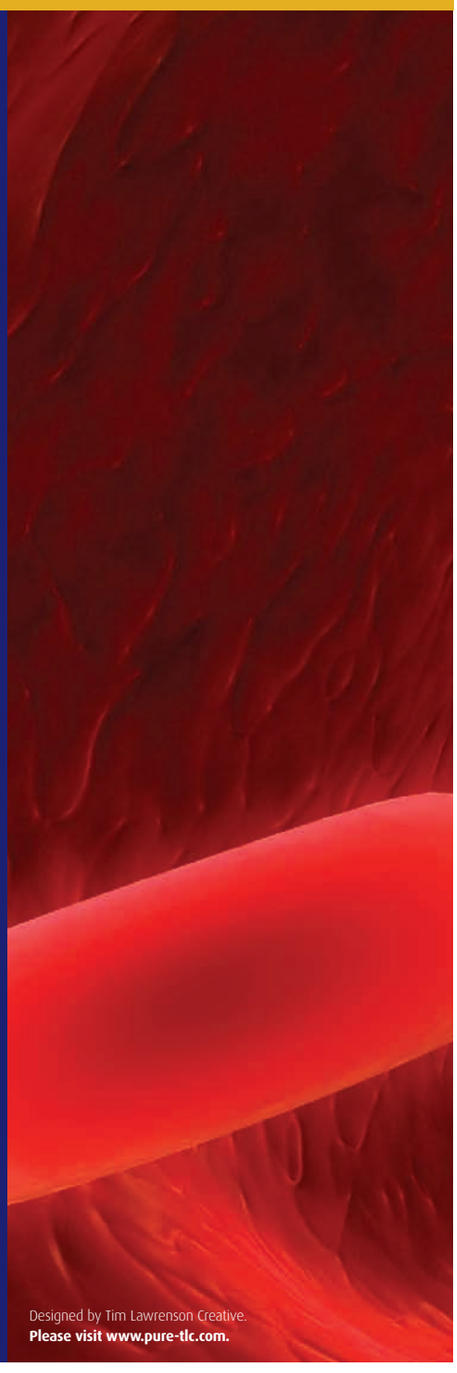

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